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ARCHIVES OF SURGERY

VOLUME 23 JULY, 1931 NUMBER 1

# OSTEOCHONDRITIS DISSECANS

## A RÉSUMÉ OF THE THEORIES OF ETIOLOGY AND THE CONSIDERATION OF HEREDITY AS AN ETIOLOGIC FACTOR *

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AND

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PHILADELPHIA

Osteochondritis dissecans is a noninfectious process involving the articular cartilage and the subchondral bone of certain long bones of the extremities, which, by sequestration from the articular surface, usually produces a single foreign body or, more rarely, two, in the contiguous joint. This body is originally of an osseocartilaginous composition, but its structure subsequently undergoes alteration by the fluids in the joints. The mesial half of the articular surface of the internal femoral condyle is the site most frequently involved, but the heads of the radius, femur and humerus may also be the sites of the process. Osteochondritis dissecans occurs preeminently in youth, and most commonly in the tall, rapidly growing boy.

### OTHER TYPES OF BODIES OF THE JOINTS

Free bodies within the joints are encountered in conditions other than osteochondritis dissecans. All such bodies are grouped under the common heading of corpora libera articulorum or "joint mice."

1. Free bodies of traumatic origin may arise in otherwise normal joints. Cartilaginous or bony "mice" occasionally follow severe trauma to the bones comprising a joint. Pieces of normal cartilage or bone may be torn loose and appear free within the joint. An example is found in fractures of the semilunar cartilages. Severe traumas to the joints are frequently followed by the periarticular formation of bone.

2. Free bodies may appear in joints that are the site of arthritis deformans. These bodies arise by the traumatic or necrotic freeing of articular cartilaginous plaques, hypertrophic bony spurs, bony joint papillae, metaplastic cartilage or hypertrophic fibrinous synovial villi. These bodies usually are present in large numbers, vary greatly in size and frequently present a mulberry-like surface.

3. The polypoid bodies present in the hypertrophic type of arthropathic tabetique (incorrectly known as Charcot's joint) present the same

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general etiology noted for free bodies appearing in the joints in arthritis deformans.

4. Masses of uric acid salts, usually sodium biurate, of various sizes are frequently found free within gouty joints.

5. Osteomyelitic sequestrums occasionally appear within a joint.

6. Parts of tumors of the capsule in chondromatosis of a joint sometimes are found free within the joint.

7. Fibrous or lipomatous joint papillae (lipoma arborescens) occasionally become loosened and form free bodies in the joints.

8. Parts of hypertrophic synovial villi following a synovitis may be severed from their base by trauma or necrosis and appear within the joint as free bodies. When these villi or papillae contain cartilaginous foci or "rests," the process becomes known as "synovitis prolifera cartilaginea."

9. Corpora oryzoidea (rice bodies) arise as a result of tuberculous involvement of the structures adjacent to a joint. They are numerous, and their structures are those of fibrinoid lamellated masses.

10. Following hemorrhage into, or inflammation of, a joint, masses of fibrin may result and lay free within the joint.

11. Foreign bodies from external sources may become lodged within the joint.

## THEORIES OF ETIOLOGY

A careful study of the literature of osteochondritis dissecans discloses many theories of etiology. This literature is grouped into two large divisions: (1) papers in which trauma is set forth as the chief etiologic factor and (2) papers in which factors other than trauma are advanced as causative agents.

The papers emphasizing trauma as the cause of osteochondritis dissecans will be presented first; the various other theories of etiology will then be considered in chronological order.

The first description of loose bodies in joints was made by Pechlin, about 250 years ago.

*Trauma as a Causative Agent in Osteochondritis Dissecans.*—Monro (1726) advanced the theory that loose bodies within the joints were of traumatic origin. In this belief he was supported by Riemar (1770) and by Haller (1776).

In 1848, Rainey "observed that fragments of cartilage and bone detached within the joint by trauma continued to grow and become sizable loose bodies."

That the production of joint mice arose only through trauma or arthritis deformans was contended by Brodhurst, in 1861, and was upheld by Poncet, in 1881.

Kragelund (1884) assumed a trauma of the "bone-cartilage region," followed by the demarcation and separation of a portion of this area by a chronic inflammatory process. In 1887, this author, experimenting on the knees of cadavers, corroborated the opinion of Paget by finding it "impossible to detach a fragment of articular cartilage simply by a blow; an area was loosened in this manner, but in order to separate it, a prying force had to be applied." Burghard (1892) produced a complete separation of a piece of articular cartilage by an oblique blow on the internal condyle when the knee was flexed.

Conflicting results were obtained by Hildebrand (1896), who found it impossible to produce permanent free bodies in the joints of animals by the surgical detachment of fragments of either cartilage or cartilage and bone.

Preiser (1898) considered osteochondritis dissecans to be the result of static imperfection. Harris (1901) found that "in my subsequent study of these cases there is almost no one who reports a case who does not reach the conclusion that König was wrong."

Boerner (1903) insisted "upon a purely mechanical basis" for the origin of these bodies. Codman (1903), from experimental work on cadavers, concluded that "the life history of the loose cartilage must comprise two injuries, one to depress it, and one to free it."

Cornil and Coudr-v (1905) found that bodies of traumatic origin produced through experiment in animals became united to the articular extremity of the bone or to the synovial membrane of the joint.

Rimann (1905), following experiments on both dogs and goats, stated, "there is neither a secondary nor a primary osteochondritis dissecans. True, free joint bodies arise only upon a traumatic basis."

Ludloff (1908) advanced the following theory:

> The loose bodies arising from the lateral surface of the mesial condyle result from injury to the arteria genu media at the point where it perforates the posterior capsule of the joint, and before it enters the bone at the seat of insertion of the posterior crucial ligament. The resulting circulatory disturbance leads to necrosis of the area of bone supplied by the injured vessel. The necrotic bone is gradually separated as the result of insufficient nutrition.

Axhausen (1914) indicated that the vascular system might play a slightly different rôle than that expressed by Ludloff. He assumed:

> As the result of the impaction from the opposing articular surface, the blood vessels to the part are damaged, either with or without partial fracture, according to the severity of the violence. This leads to necrosis of the area supplied by the damaged vessels. Instead of creeping substitution of the necrotic bone or bone and overlying cartilage, as would result in case of aseptic bone necrosis in other regions, there forms a zone of absorption resulting in gradual separation and eventual extrusion of the dead portion of the joint.

Friedrich (1913), Bernard (1925), Brackett and Hall (1927) and Schumm (1928) all favored the theory of traumatism.

Fisher (1920) stated:

> Not infrequent detachment by indirect injury is produced by violent tension upon the posterior ligament of the knee joint, which is attached immediately adjacent to the articular margin and is powerfully reinforced by the tendons of the gastrocnemius and semimembranosis.

To strengthen his argument in regard to the factor of trauma, Fisher chiseled off a small piece of articular cartilage together with a portion of the underlying bone from the femoral condyle of a rabbit. "The portion was completely detached and pushed up into the supra-patellar recess of the joint," which was then closed. Five weeks later, the loose body was removed. On microscopic examination he found the following changes:

> The majority of cartilage cells are perfectly healthy but many of the bone corpuscles are dead. The latter must have died after detachment, therefore it seems reasonable to assume that the bone corpuscles in the classical type of loose body have also died after the detachment by trauma, and that their death is not due to any morbid pathological process. This fact cannot therefore be adduced in favor of some pathological process such as "quiet necrosis."

Kappis (1920) pointed out that in the knee and the elbow, which are the common seats of loose bodies, tangential and rotating forces may act on the convex surface of the condyle and fissure or partially or completely detach portions of the articular end. He thinks that loose bodies arising from the patella are the result of tangential forces. To explain the traumatic origin in the absence of serious injury, he assumed a predisposition as the result of disease or congenital disturbance of the articular cartilage. "Articular cartilage has no nerve supply and the underlying spongy bone is extremely insensitive. This should permit of the occurrence of fracture with little or no serious injury."

Phemister (1920) believed "that osteochondritis dissecans in all cases is a fracture caused by mechanical relationships or slight, unnoticeable trauma which results in either complete or partial separation of the piece in question."

Hellström (1922) assumed:

> The joint mice in osteochondritis dissecans are the result of a subchondral impression fracture. Excessive effort due to special structural conditions of the knee joint may lead to the production of these fractures. Hence, individual predisposition plays a part in the development. The failure of firm healing of the fracture completes the clinical picture. There is no spontaneous dissecting osteochondritis in König's sense, and therefore it is best to give up the idea entirely. In giving a legal opinion on the so-called dissecting osteochondritis, the condition must be regarded as an occupational disease produced by trauma.

Freiberg (1923), by a roengenographic study of five cases and the knees of a number of cadavers, found the following:

> It was quite easy, even where the tubercle was not long, to make it impinge upon the posterior crucial ligament when the knee was flexed and the tibia rotated outwards. Where the tubercle is long the impingement occurs much sooner, and it seems easily conceivable that it might take place with enough force to damage a small vessel were this to be found just in the right place. For the present, at least, it would seem as if we must look upon this interesting condition as the result of trauma.

Sommer (1923) reported:

> The exciting cause akin to necrosis of the cartilage in animal experiments, is contusion that does not lead to death of the cartilage, but introduces the process of dissection and separates the contused tissue from the healthy portions of the joint by aseptic dissection.

Burckhardt (1923) claimed:

> The chief reason for many misunderstandings on this question lies in the fact that so far we have been unable to form any satisfactory idea of the nature of the mechanical forces on which it is based, so that it is not known whether the traumas reported in the histories are sufficient in force to produce a fracture from pressure or from bursting.

Burckhardt experimented on cadavers and showed that injury of the median condyle takes place from pressure of the patella. In an incipient case the patella, as a result of fixation by the quadriceps, was pushed with great force against the underlying structures. The amount of this force was calculated according to the laws of mechanics, and it was shown that sufficient force could be derived from contraction of the quadriceps extensor muscle to produce a fracture. That a trauma with such force should cause as little pain as is generally reported is explained by the absence of sensory fibers in the cartilage of the joint. The question of the etiology of joint mice is, therefore, only a problem of the mechanics, of joints and muscles and the histologic pictures are the expression of a reaction of the tissues to a trauma under certain mechanical and anatomic conditions.

Schmidt (1924) demonstrated on the cadaver that at the level of the condyles the cartilage in a joint was more easily injured by a tangential than by a vertical force. He further ascertained the varying positions of the patella when the leg was internally and externally rotated from a position of 60 degrees flexion. He found that when the leg is rotated outward the patella comes in contact with the external condyle; when it is rotated inward, it comes in contact with the internal condyle. In this gliding from one condyle to the other, the tip of the patella moves through a greater arc than does the base. With the leg flexed at 90 degrees or more, the upper border of the patella lies above the condyles.

Schmidt claimed that condylar fragments are broken off by impact between the patella and the condyles following sudden rotations of the leg when in flexion.

According to Phemister (1924):

> In many instances there is a history of traumas with impaction, either alone or combined with rotation or hinge motion in the joint. . . . In dogs, pieces of bone and cartilage chipped off and reinserted in their beds, become reattached in practically every instance. They are usually absorbed and disappear completely in a few months.

The same author was unable experimentally to produce loose bodies within joints by creating necrotic areas in the articular cartilage or subchondral bone by the insertion of radium needle.

Timbrell Fisher (1924) pointed out:

> Trauma to the epiphysis will produce a low grade type of inflammatory process in a certain area which thus has lowered vitality, and which may be gradually exfoliated.

Häuptli (1924) stated:

> Osteochondritis dissecans is a purely traumatic, complete or incomplete detachment of cartilage or bone-cartilage bodies in the knee or elbow. If bits are incompletely broken off, the processes of healing in the fragments lead to a rudimentary callous formation and now and then to consolidation. The frequent traumas of daily life with the physiologic movements of the knee bring about entire separation of the detached bodies. A necessary predisposition to the disease is created, on the one hand, by a special bone configuration in the joint, and on the other hand, by hypothyroidism (hyperthyroidism?) and late rickets, but most of all by an arthritic constitution.

Leb (1924) disagreed with the authors who believe the following to be true:

> A chronic inflammatory process must be declined as the fundamental cause of the illness in default of actual proof. No proof has been produced for the so-called osteochondritis dissecans as an independent, chronic inflammatory procedure. Its symptom-complex could indeed be kept within the bounds of the form of illness of arthritis deformans, of the specific inflammatory process in bone, not, however, separated from every form of traumatic joint mouse formation. The harmony of the clinical and roentgenological pictures as well as the "anamnese" does not exclude the traumatic damage in the course of the daily work, and forces one to the assumption that the illness described as osteochondritis dissecans is subordinated to the domain of joint fractures.

Von Dittrich (1925) thought "that osteochondritis dissecans is the result of mechanical and functional traumatic influence."

Balensweig (1925) believed that osteochondritis dissecans was the result of "an osteochondral fracture of the external femoral condyle as a result of cross strain, aided by the pull of the anterior crucial ligament."

Wolbach and Allison (1928) offered an explanation of its etiology:

> The separation was the effect of mechanical pressure on a portion of the articular cartilage with underlying cancellous bone bridging a "cyst." This pressure probably was intermittent as occasioned by variation in functional performances of the joint, and probably was the result of stresses operating roughly in the long axis of the bone and laterally in the anterior-posterior direction. . . . There are two essentials to our explanation; one, a sufficient loss in the condyle of cancellous bone to weaken materially the support of the articular cartilage as a whole; the other, the presence of a "cyst" immediately below the articular cartilage in a position subject to vertical and horizontal stresses. The rarity of typical instances of osteochondritis dissecans of the femur suggests that our observation, even if dependent on the fortuitous existence and distribution of "cysts," may apply to other examples.

Richards (1928), in describing the roentgenologic picture of osteochondritis dissecans, wrote:

> In one of our cases the lesion was found in both knees of the individual, and in both of these, the mesial tubercle of the tibial spine was elongated, thus suggesting a purely local process due to this peculiarity.

*Causative Agents Other than Trauma in Osteochondritis Dissecans.*—Many investigators do not consider trauma the causative agent in osteochondritis dissecans.

John Hunter (1793) believed that the formation of cartilaginous bodies in joints was due to extravasated blood which assumed the nature of the parts into which it was effused.

Rokitansky (1851) stated that "bodies composed of bone and cartilage might arise from the articular serosa, representing an excessive development and ossification of isolated nodules of cartilage." Laennec (1854) indicated that an arthritis was the basis, while Broca (1854) assumed a dry sequestration process as the cause of loose bodies in joints.

Klein (1864) disagreed with these modes of origin. It is "most likely a question of a spontaneous demarcation of part of the joint of the femur."

Paget (1870) could not conceive how pieces of articular cartilage could be detached from living bone by trauma; ". . . these loose bodies are sequestra, exfoliated after necrosis of injured portions of cartilage, exfoliated without acute inflammation."

Koch (1879), performing experiments on embolic necrosis of the bone, proved to his own satisfaction that loose bodies were the result of "the obstruction of the entire capillary area of nutrition."

Poulet and Vaillard (1885) believed that osteocartilaginous bodies were due to "a spontaneous necrosis and a secondary loosening."

In 1887, König published his article, "Ueber freie Körper in den Gelenken," in which he described one type of loose bodies within joints; after his clinical and anatomic studies of these he felt justified in segre-

gating them into a pathologic entity which he termed osteochondritis dissecans. He pointed out that this condition may occur in any joint, but that it most frequently involves the knee and elbow joints in young persons. He was unable to elicit a definite history of trauma in any of his cases, and having excluded arthritis deformans, acute and chronic suppurative or tuberculous osteomyelitis and tabes as the cause of the loose bodies, he concluded that it was a question of a "blasting" of a piece of the surface of the joint by a "dissecting osteochondritis," which resulted in the "severance of a piece of the joint surface without otherwise noteworthy damage to the joint itself." He did not deny that trauma may be a factor in the production of "corpus mobile," but only so far as it gives rise to the "occasion of bringing into prominence the complaints of a joint body which had already existed for a long time." He admitted, however, that "the etiology of this pathological-anatomical process remains obscure." The appearance of König's article occasioned much controversy.

Humphrey (1888) was skeptical about trauma as an etiologic factor, as it would require "a very extraordinary and violent accident that would break off into the knee joint a piece of articular cartilage." He cited as the etiology, descriptions of pathologic processes now established as those associated with arthritis.

Halstead (1895) was inclined to agree with König "that few, if any" of the loose bodies found in otherwise normal joints "are the direct result of violence."

Barth (1896) considered that proof for the existence of osteochondritis dissecans as an entity was lacking, and that König's clinical and operative observations were of doubtful value. He claimed that only by trauma and arthritis deformans could loose bodies arise in joints. Barth excluded a necrotic process as a causative agent by demonstrating living cartilage in free bodies within joints. However, he failed to consider that bodies within joints could receive nutriment from the synovial fluid. Lindenstein (1906) and Brehm (1913) reported cases which they believed corroborated Barth's opinion.

Freiberg and Wooley (1910), reporting a doubtful case of osteochondritis dissecans, agreed with Wollenberg's theory of vascular changes secondary to arthritis deformans as being the cause of free bodies within joints.

Weil (1912) reported two cases of bilateral symmetrical osteochondritis dissecans. He considered Ludloff's theory of inflammatory foci the explanation for the bilateral symmetry of the lesions.

Colvin (1920) believed the process to be infectious, while Reiger (1920) considered it one of infarction secondary to a fat embolus.

Buchner and Rieger (1921), in order to disprove the traumatic theory, showed that 184.3 Kg. of force was necessary for the loosen-

ing of a piece from the femoral condyle by extension of the crucial ligament and 614 Kg. by pressure of the patella against the femoral condyle.

Nussbaum (1923), after studying the possibility of the embolic origin of free bodies in the knee joint, came to the conclusion that such a theory was not tenable, as the arteria genu media was not an end artery. Axhausen (1924) disputed Nussbaum's conclusions:

> The theory of the embolic origin of joint bodies rests on three pillars: (1) mycotic-embolic closure of an epiphyseal artery may lead rapidly to epiphyseal necrosis. (2) The bacteria deposited may be vanquished by the body so that an infection does not take place and the necrosis remains aseptic. (3) Joint bodies may develop in situ from the aseptic epiphyseal necrosis by a process of demarcation. Nussbaum's statements are concerned exclusively with the first and third possibilities. On account of the extent of his examinations, his judgment must be regarded as especially valuable on the question of whether an epiphyseal necrosis may develop from embolic occlusion of a vessel. But it is highly noteworthy that he has a tendency to answer this question in the affirmative for the lower end of the femur. To be sure the epiphyseal arteries are not terminal arteries in an anatomic sense, as fine lateral connections can be demonstrated. But these anatomic findings do not prove that the functional capacity of the fine connections is sufficient to ensure the nutrition of the epiphyseal region on closure of the chief artery. Observations in osseous tuberculosis seem to prove that the lateral connections do not suffice for this, and that therefore, the epiphyseal arteries are "functional" end arteries, and if they are occluded there must be an interruption of nutrition in the area they supply. The tuberculous wedge-shaped necrosis in the lower epiphysis of the femur, with its apex directed toward the diaphysis, may very well correspond to a single epiphyseal vessel area. Nussbaum's admission that the cone shaped sequestrum of the epiphysis may be brought about even without end arteries in the anatomic sense, is a valuable support for the first theory; it does not argue against but in favor of, an embolic genesis. His evidence against an embolic origin is directed solely against the third theory. The point of embolic vessel occlusion is not at a site of separation but much higher up, probably at the same place where Nussbaum assumes occlusion in tuberculous embolic wedge shaped necrosis. The theory of the embolic origin of joint bodies cannot be regarded as shaken or even answered by Nussbaum's anatomic examinations. On the contrary, they give the theory a certain support, as they confirm the possibility of the development of epiphyseal wedge shaped necrosis by the embolic route.

In further consideration of the rôle of the vascular system, Axhausen (1924) stated that the primary lesion is a necrosis of the epiphysis. This is followed by a proliferation of the surrounding tissues that penetrate into the dead bone, and may end with complete reorganization. This regeneration is interrupted by a compression fracture of the diseased epiphysis, which is frequently erroneously considered as the beginning of the disease. The fracture is limited everywhere by dead tissue, and therefore healing is impossible. The ends rub against each other and produce "bone flour." Instead of a comparatively quick substitution, a slow resorption sets in. The cartilage is not yet severely changed, but the necrotic part of the epiphysis

begins to be demarcated from the remaining bone by a layer of granulations or of older connective tissue. A slight injury may free the necrotic part in the elbow or knee joint, because these are broad and especially exposed to such injuries. As to the primary cause of the necrosis, he admits the possibility of tortion of blood vessels, especially in dislocations, but believes that benign infected emboli are more probable. In 1925, this author concluded that "the cause of the epiphyseal necrosis, which is the basis of all these joint diseases, is not yet proven. However, according to new investigations, I maintain their explanation as bland mycotic embolic necrosis." Lehmann (1925) did not agree entirely with Axhausen. "The theory of Axhausen, that a pathological fracture lies at the bottom of osteochondritis dissecans, is the most plausible; on the other hand, the assumption of a bland, necrotic embolus has been rejected because every provable case is without it." According to Walter (1926), "the König-Axhausen theory of emboli as the cause of subchondral bone necrosis experiences a corroboration through such cases in which multiple necrosis appears in reference to 'Infecktionskrankheiten'." Besides a bilateral osteochondritis dissecans of both knee joints in a man, aged 22, he found a typical foci in the capitulum radii.

Konjetzny (1924) found an obvious endarteritis obliterans. "Perivascular round cell infiltration which was found here and there, may be thought of as an inflammatory origin."

According to Kroh, Lieck is of the opinion that the condition is due to "Hormonale Störung der inneren Sekretion."

Bernstein (1925) suggested:

> There must be some underlying constitutional factor, probably a congenital predisposition of the joint tissues, which is indispensable in the formation of loose bodies in the knee joint. It would also account for the occurrence of loose bodies in homologous joints in the same patient. Granting the existence of such an hereditary predisposition, any exciting causes, such as traumatism, inflammatory changes would act as an exciting cause for the formation of loose bodies in such a joint.

Heine (1927) accepted Axhausen's theory as being, "theoretically at least, the most likely hypothesis," and at the same time rejected Rieger's theory of an arterial fat embolus as "not only an improbable but an impossible hypothesis."

Moulonguet (1929) considered:

> A very definite relation between the dry arthritis and the osteochondritis dissecans; in the exfoliation of the cartilage, the partial necrosis of the epiphysis may be the lesions of dry arthritis which, in miniature, produce the process of osteochondritis dissecans.

## REPORT OF CASES

CASE 1.—*History.*—C. H.,[1] a tall, white boy, aged 15, was first seen in the outpatient department on May 10, 1928. He complained of limitation of motion of the joint of the left knee. For the past four years the patient had had intermittent disability of the left knee joint. This disability consisted of slight limitation of motion, occasional pain and infrequent "locking" of the knee joint. The "locking" was accompanied by the slight swelling of the soft parts on the inner side of the joint. The patient was always able to "unlock" the knee without

Fig. 1 (case 1).—Left knee joint; the loosened osteocartilaginous body is shown on the mesial aspect of the internal femoral condyle.

assistance. No history of trauma could be obtained to account for the original attack. One week previous to admission, the patient was kicked above the left knee. The part became swollen and painful; the patient was unable fully to extend the leg or to flex it beyond a right angle.

*Examination.*—The patient walked with a limp of the left lower extremity. Flexion stopped at 90 and extension at 165 degrees. Swelling and induration about

1. From the Philadelphia Orthopaedic Hospital and Infirmary for Nervous Diseases, surgical service of Dr. William J. Taylor.

the knee were absent. A point of tenderness was demonstrated at the anterior margin of the tibial attachment of the left internal lateral ligament.

A diagnosis of osteochondritis dissecans was made and confirmed by a roentgenogram (fig. 1).

*Treatment.*—Normal motion was restored to the knee joint by a course of baking and massage.

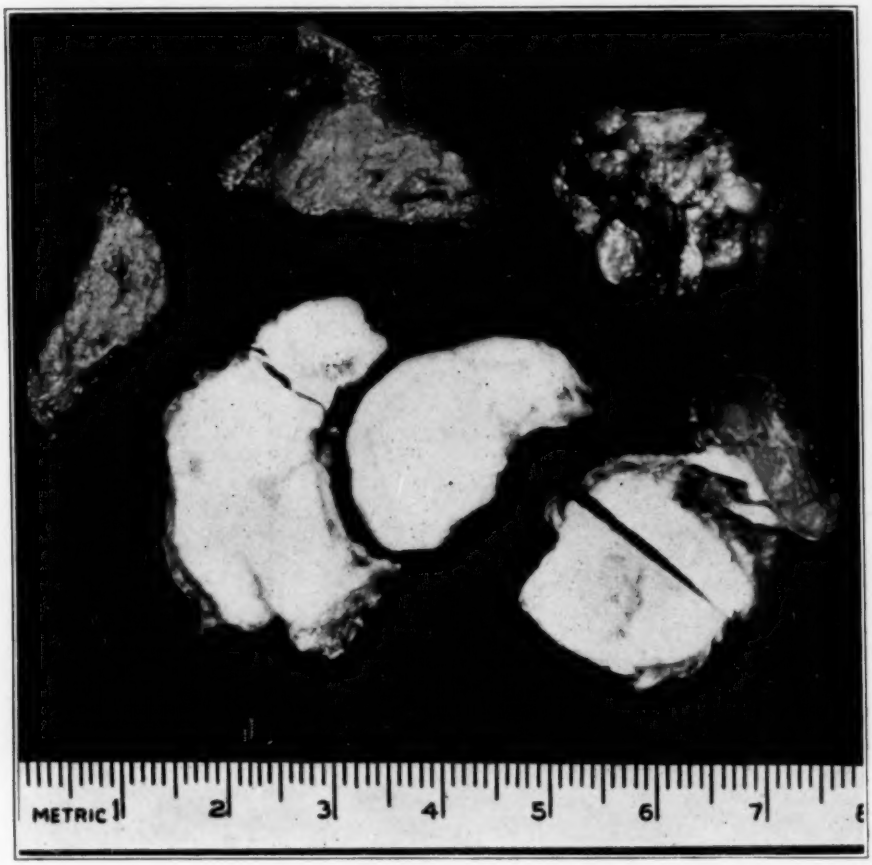


Fig. 2 (case 1).—Material removed from the inner compartment of the left knee joint. The upper three bodies are tags of hypertrophic synovial fringes. Of the lower three bodies, the middle one with the rounded edges was free within the joint; the other two, while loose, were still attached to the surface of the condyle, and formed the outer edges of the crater from which the free body was sequestrated.

*Second Attack.*—When next seen on October 4, the patient's left knee was again locked in flexion at 45 degrees. During the previous evening, "for no apparent reason," the knee joint locked. Marked tenderness and swelling were present over the internal anterolateral surface of the joint.

Operation was advised, and the patient was admitted to the hospital. He was operated on the following day.

*Operation.*—With the patient under nitrous oxide-oxygen anesthesia, a straight longitudinal incision was made to the inner side of the patella, and the inner compartment of the left knee joint was exposed. A large oval body with smooth rounded edges was found lying free within the joint. This body was removed, together with two irregularly shaped pieces of bone and cartilage which were partially separated from the inferior articular surface of the internal condyle. Several tabs of hypertrophied synovial villi were also removed. The wound was closed without drainage.

The patient was discharged on the fifteenth day after operation. He was free from pain and had a normal range of motion in the left knee joint. When last seen, three months after operation, there was no disability.

*Gross Examination.*—At the time of operation the conditions within the knee joint were carefully observed. There was a slight increase in the amount of synovial fluid. The internal semilunar cartilage was intact. No evidence of infection was noted.

The foreign body which was removed was ovoid and of the size shown in figure 2. It was glistening white, with smooth, rounded edges. The body consisted of a thick layer of articular cartilage and a thin, partially absorbed layer of subchondral bone.

The condition of the inferior surface of the internal femoral condyle was of interest. To the mesial side of the condyle and at a point near the attachment of the posterior crucial ligament was seen a large ovoid crater extending through the articular cartilage and into the bone of the condyle. This depression corresponded to the size and shape of the foreign body which was found free in the joint. The assumption is made that the foreign body was an extrusion of cartilage and bone from the site of the crater and that the crater was made by this extrusion. The margins of the crater were rounded; its walls were sheer; its depth was slightly greater than the thickness of the foreign body. The margins of the crater were loose on the anterior, internal-lateral and posterior sides. At operation, the already loosened cartilage about the crater with its attached bone was removed in two irregularly shaped pieces. The cartilage was friable and tore from its attachment to the remaining articular cartilage with ease, leaving a sloping, irregular and tufted edge. The defect which was produced by the removal of these two pieces of semidetached cartilage and bone, together with that of the crater, occupied practically the entire mesial half of the articular surface of the internal condyle.

*Laboratory Examination.*—Repeated blood counts, chemical determinations of the blood and urinalyses were consistently normal. The Wassermann reaction of the blood was negative. Bouillon and agar slant cultures of the fluid in the joint, a piece of hypertrophied synovial villi, and a portion of foreign body were free from bacterial growth after eight days' incubation.

*Microscopic Examination.*—The synovial villi (fig. 3) were large and their papillae broad. The surface lining consisted of a single layer of flattened cells; it was intact in some areas, but in others it was replaced by a thin, compact band of acid-staining fibrin. Immediately beneath the periphery were a large number of thin-walled blood vessels which were dilated and contained within their lumen an excessive number of polymorphonuclear leukocytes. The adjacent tissue was loose and edematous, and throughout it were scattered many plasmocytes and youthful connective tissue cells, together with an occasional polymorphonuclear

leukocyte. In the vicinity of the blood vessels were seen collections of lymphocytes. The deeper tissue had a normal fibro-areolar structure.

The diagnosis was: subsiding acute inflammatory changes in hypertrophied synovial villi.

The section of the foreign body consisted chiefly of cartilage to the under surface of which was adherent a small amount of bone. The cartilaginous surface of the section was smooth, and the nuclei of the cartilage cells in the first zone lay parallel to the marginal edge; in the second zone, the nuclei occupied an indefinite position, whereas in the deepest zone, they were arranged at right angles to the surface. The cartilage was viable and of normal composition.

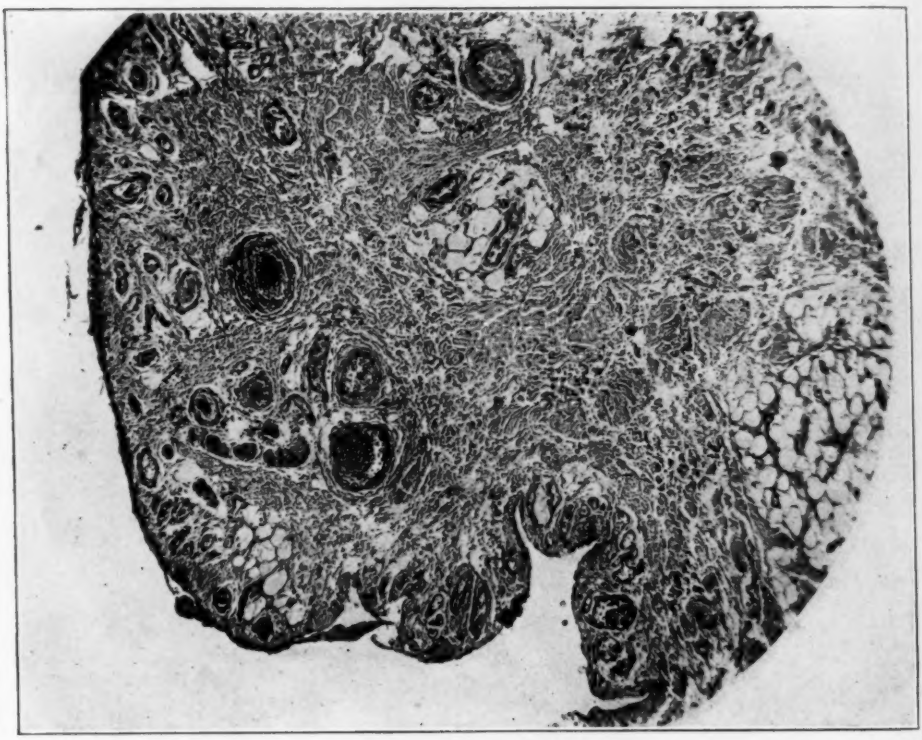

Fig. 3 (case 1).—Photomicrograph of the hypertrophic synovial villi removed from the left knee joint. Hematoxylin eosin; × 61.

The bone present in the free body was small in amount, and on section showed by its poor staining quality marked decalcification (fig. 4). No evidence of osteoblastic activity was found. The bone cells were few in number and necrotic. The margins of the trabeculae were irregular and fuzzy, while the presence of many marginal lacunae gave evidence of osteoclastic activity, although no osteoclasts were found.

The diagnosis was: necrotic subchondral bone undergoing decalcification and absorption.

In addition to the patient, two other male members of his family were said to have suffered from the same type of disability. These persons, the patient's father and paternal uncle, were examined. The records of their cases, which follow, verify and confirm the diagnosis of osteochondritis dissecans.

CASE 2.—H. E. H., a white man, aged 49, father of the patient, when 12 years of age first noted a slight, intermittent, dull pain in the joint of the left knee, accompanied by limitation of both flexion and extension. No history of preceding

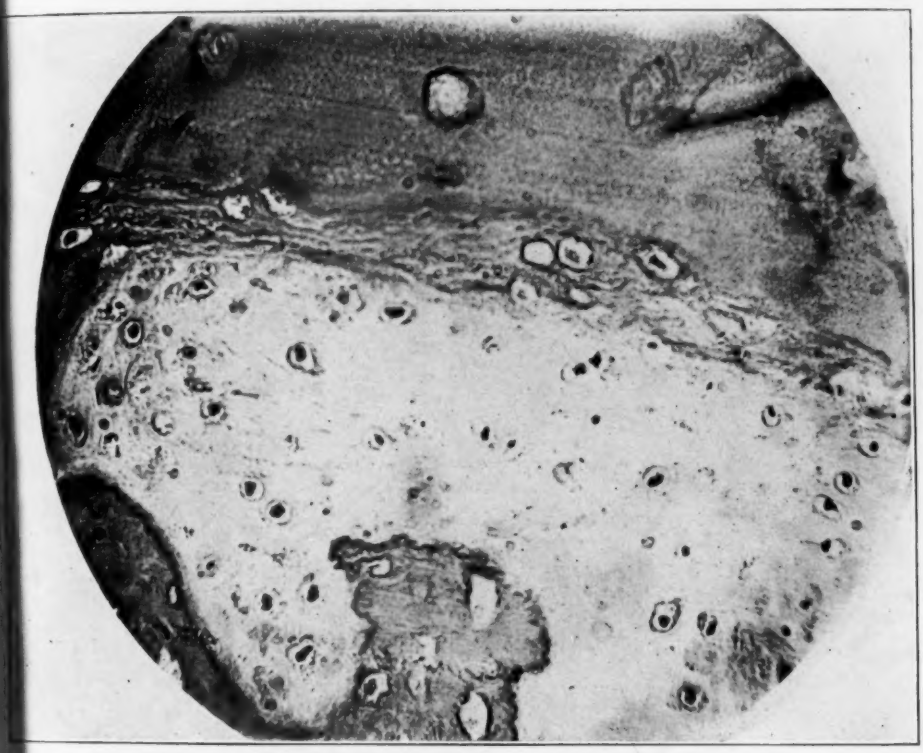

Fig. 4 (case 1).—Photomicrograph of the osteocartilaginous body removed from the left knee joint. Hematoxylin eosin; × 328.

trauma could be obtained. Occasionally, following strenuous activity, the knee would swell and lock, but the patient was able to free the obstruction. Operation for the removal of a foreign body in the knee joint was recommended but refused. The condition persisted for twenty years. An apparent cure was effected by the spontaneous extrusion of the foreign body from the knee joint into the surrounding soft tissues.

At the present time, the patient is free from pain and disability. Examination revealed the presence of a hard mass beneath the outer edge of the quadriceps extensor femoris muscle just above the external condyle of the femur. A roentgenogram demonstrated this mass to be a piece of bone or cartilage, and in addition

showed that a smaller particle of bone or cartilage lay in the midanterior portion of the knee joint apparently attached to or embedded in the capsular ligament (fig. 5).

CASE 3.—G. W. H., a white man, aged 46, paternal uncle of the patient, when about 15 years of age noticed the development of "locking" of the joint of the right knee without a history of preceding trauma. The disability continued intermittently for thirteen years. The periods of limited function of the joint became more frequent and lasted longer as he grew older. Walking upstairs or climbing a hill predisposed to "locking" of the joint. Medical aid was sought, and operation was advised.

Fig. 5 (case 2).—Lateral view of the left knee joint. Two foreign bodies are seen; the upper lies beneath the lateral border of the quadriceps extensor; the lower lies in the midanterior portion of the joint.

On July 13, 1912, the patient was admitted to the Jefferson Hospital. An excerpt from the hospital records reads: "Diagnosis: floating body in the right knee joint. Physical examination negative, except the right knee which is slightly swollen at the inner aspect; the patella appears to float in fluid. The knee joint was opened by Doctor Despard under general anesthesia and a medium sized piece of bone removed. The patient was discharged in good condition on the sixteenth day after operation."

Since operation, the patient has been free from pain and disability. Roentgenographic examination of the right knee joint (Oct. 1, 1928) failed to show any abnormality of the bones or cartilage comprising the joint.

CASE 4.—*History.*—D. S. P.,[2] a white boy, aged 19, tall and well developed, was first seen on April 5, 1927. Three weeks previously, without assignable cause, the right knee became swollen. Any sudden twist caused pain in the region of the external lateral ligament, and several times a day the knee joint would "lock" and the patient could extend the leg only after manipulation. The discomfort increased in severity.

Fig. 6 (case 4).—Right knee joint; an osteocartilaginous body is loosened from the inferior surface of the internal femoral condyle.

*Examination.*—Motion at the knee was free; there was a slight amount of swelling present, and a point of tenderness over the attachment of the external lateral ligament was found.

A roentgenogram disclosed a large, partially detached sequestrum from the midarticular surface of the right internal femoral condyle (fig. 6).

*Operation.*—On April 20, with the patient under general anesthesia, the foreign body consisting of articular cartilage and subchondral bone was removed. The patient made an uneventful recovery.

2. Cases 4 and 5 concern private patients of Dr. DeForest P. Willard.

When examined in February, 1930, the patient complained of infrequent pain in the left knee. A roentgenogram revealed the presence of a solitary foreign body in the inner compartment of this knee.

CASE 5.—*History.*—W. P., Jr., a brother of D. S. P., white, aged 19, over 6 feet in height and weighing but 150 pounds (68 Kg.), was first seen on July 25, 1925. For several years he had complained of pain in both knees and in the dorsal and lumbar portions of the spine, following exercise.

*Examination.*—The left lower extremity was one-half inch (1.27 cm.) shorter than the right. A slight lumbar scoliosis to the left was present; both feet were pronated; posture was poor and the musculature weak.

Fig. 7 (case 5).—Roentgenogram showing the presence of a loosened osteocartilaginous body from the inferior surface of the left internal femoral condyle.

When next seen, on Jan. 11, 1927, the patient complained of pain in both knees but more especially in the left, and frequent inability fully to extend the left leg. The joint of the left knee at times became swollen.

There was a slight grating but no swelling in the left knee joint. The ligaments were somewhat relaxed, and there was pain on pressure over the internal lateral ligament.

A small sequestrum from the middle portion of the articular surface of the internal femoral condyle was shown by roentgenogram to lie free in the joint of the left knee (fig. 7).

## HEREDITY AS AN ETIOLOGIC FACTOR

The involvement by osteochondritis dissecans of more than one joint in the same person is uncommon. Bernstein, Blanco, Richards and Walter reported cases in which more than one joint in the same person was involved. When more than one joint is the site of osteochondritis dissecans, the involvement is frequently found to be bilateral.

Few references are made to heredity and familial or congenital factors as possibly being responsible for the development of this condition. Rieger spoke of "a predisposition." Kappis claimed that there may exist a congenital disturbance of the articular cartilage predisposing it to injury. Bernstein, in reporting the presence of osteochondritis dissecans of both knees of two sisters and a brother, stated that the disease is probably hereditary.

From a consideration of the cases here reported, it would seem that heredity should be considered as an etiologic factor in the occurrence of osteochondritis dissecans.

## SUMMARY

1. The various theories of the etiology of osteochondritis dissecans found in the literature are abstracted.

2. Five case reports are given in which osteochondritis dissecans of the knee joint was found in various members of the same family, (*a*) in three men of one family; son, father and paternal uncle, and (*b*) in two brothers, in one of whom there was bilateral involvement.

## CONCLUSION

Heredity operates as an etiologic factor in the occurrence of osteochondritis dissecans.[3]

## BIBLIOGRAPHY

The bibliography here given was selected from 365 articles, and with the exception of 2 articles which were not available to us, we believe comprises the literature on the subject of osteochondritis dissecans. All the articles here listed have been abstracted.

3. A discussion of the histologic similarity of osteochondritis dissecans to other "aseptic necroses" of the bone does not fall within the province of this paper. But it is felt that there is no histologic difference between osteochondritis dissecans and that large group of clinical entities thus far designated by the names of their describers. The fact that the condition is noted in the os calcis, the semilunar of the wrist, the tarsal scaphoid, the anterior tubercle or the distal epiphysis of the tibia, the epiphyses of the femur, radius, humerus, vertebra or of the metatarsals does not make of a single pathologic process many clinical diseases.

Archer, V. W., and Peterson, C. H.: Osteochondritis Dissecans, South. M. J. **23**:611, 1930.

Axhausen, G.: Ueber einfache aseptische Knochen-und Korpelnekrose, Chondritis dissecans und Arthritis deformans, Arch. f. klin. Chir. **99**:519, 1912.

——Die Entstehung der freien Gelenkkörper und ihre Beziehungen zur Arthritis deformans, Arch. f. klin. Chir. **104**:581, 1914.

——Bemerkungen und Beiträge zur Frage der Entstehung der freien Gelenkkörper, Arch. f. klin. Chir. **114**:1, 1920.

——Zur Entstehung der freien Solitärkörper des Kniegelenks, Deutsche med. Wchnschr. **46**:825, 1920.

——Ueber Vorkommen und Bedeutung epiphysärer Ernährungs-unterbrechungen beim Menschen, München. med. Wchnschr. **69**:881, 1922.

——Bemerkung zum Vorträge Lehrmann über Osteochondritis, Zentralbl. f. Chir. **51**:24, 1924.

——Ueber die Osteochondritis dissecans Königs, Klin. Wchnschr. **3**:1057, 1924.

——Ueber den Abgrenzungsvorgang am epiphysären Knochen (Osteochondritis dissecans König), Virchows Arch. f. path. Anat. **252**:458, 1924.

——Ist die embolische Genese der freien Gelenkkörper denkbar? Beitr. z. klin. Chir. **131**:386, 1924.

——Zur Histologie und Pathogenese der Gelenkmausbildung im Kniegelenk, Beitr. z. klin. Chir. **133**:89, 1925.

Balensweig, I.: Osteochondritis Dissecans of the Knee, J. Bone & Joint Surg. **7**:465, 1925.

Barth, A.: Zur Pathologischen Anatomie der Gelenkmäuse, Zentralbl. f. Chir. **22**:977, 1895.

——Zur Lehre von den freien Gelenkkörpern, Verhandl. d. deutsch. Gesellsch. f. Chir. **25**:31, 1896.

——Die Entstehung und das Wachstum der freien Gelenkkörper, Arch. f. klin. Chir. **56**:507, 1898.

——Ueber die Entstehung der freien Gelenkkörper, mit besonderer Berücksichtigung der arthritischen Gelenkkörper, Arch. f. klin. Chir. **112**:369, 1919.

Bastos, A. M.: Ein Beitrag zur Pathogenese der Gelenkmäuse, Verhandl. d. deutsch. orthop. Gesellsch., 23rd Congress, 1929, pp. 298-313.

——and Aguilar, J. G.: Nueva contribuciön a la patogenia de los cuerpos libres articulados, Arch. de med., cir. y espec. **30**:343, 1929.

Bergmann, E.: Osteochondritis Dissecans des Hüftgelenks, Deutsche Ztschr. f. Chir. **217**:400, 1929.

Bernard, L.: Contribution à l'étude de l'ostéochondrite disséquante, Thèse de Paris, 1925, p. 161.

Bernstein, M. A.: Osteochondritis Dissecans, J. Bone & Joint Surg. **7**:319, 1925.

Blanco, Pio: Report of a Case of Loose Osteocartilaginous Bodies in the Knee Joint, J. Orthop. Surg. **3**:104, 1921.

Böcker: Ueber einen Fall von Osteochondritis dissecans genu, Zentralbl. f. Chir. **31**:136, 1904.

Boerner, E.: Klinische und pathologisch-anatomische Beiträge zur Lehre von dem Gelenkmäusen, Deutsche Ztschr. f. Chir. **70**:363, 1903.

Brackett, E. G., and Hall, C. L.: Osteochondritis Dissecans, Am. J. Orthop. Surg. **15**:79, 1917.

Brehm, O.: Zur Kasuistik der Gelenkmäuse, Deutsche Ztschr. f. Chir. **124**:81, 1913.

Broca, P.: Sur la nécrose des cartilages articulaires, quoted by Leb, A.: Arch. f. klin. Chir. **131**:425, 1924.

Buchner, L., and Rieger, H.: Können freie Gelenkkörper dürch Trauma entstehen? Arch. f. klin. Chir. **116**:460, 1921.

Burckhardt, H.: Ueber Entstehung der freien Gelenkkörper und über Mechanik des Kniegelenks, Beitr. z. klin. Chir. **130**:163, 1923.

——Diskussionsbemerkung zum Vorträge Fritz König's Osteochondritis dissecans, Arch. f. klin. Chir. **142**:141, 1926.

Burghard, quoted by Connell, F. G.: Ann. Surg. **43**:247, 1906.

Christie, A. C.: Osteochondritis or Epiphysitis, J. A. M. A. **87**:291 (July 31) 1926.

Codman, E. A.: The Formation of Loose Cartilages in the Knee Joint, Boston M. & S. J. **149**:427, 1903.

Colvin, A. R.: The Clinical Course and Pathology of an Obscure Ostitis Causing Loose Bodies in Joints, Minnesota Med. **3**:65, 1920.

Connell, F. G.: Loose Bodies in the Knee Joint, Ann. Surg. **43**:247, 1906.

Cornil, V., and Coudray, P.: Des corps étrangers articulaires et en particulier des corps traumatiques, Rev. de chir. **31**:429, 1905.

Curtis, G. M.: Osteocartilaginous Loose Bodies in the Knee Joint, S. Clin. North America **9**:415, 1929.

von Dittrich, K.: Zur Frage der Osteochondritis dissecans des Kniegelenkes, Zentralbl. f. Chir. **52**:204, 1925.

——Ueber Osteochondrolysis traumatica (Osteochondritis dissecans gen. König): Eine klinische und histologische Studie, Virchows Arch. f. path. Anat. **258**: 795, 1925.

Fischer, M.: Beitrag zur Kenntnis vom Wachstum freier Gelenkkörper, Virchows Arch. f. path. Anat. **269**:239, 1928.

Fisher, A. G. T.: A Study of Loose Bodies Composed of Cartilage or of Cartilage and Bone Occurring in Joints, with Special Reference to Their Pathology and Etiology, Brit. J. Surg. **8**:493, 1920-1921.

Fisher, T., quoted by Wolbach and Allison.

Freiberg, A. H.: Osteochondritis Dissecans, J. Bone & Joint Surg. **5**:3, 1923.

——and Woolley, P. G.: Osteochondritis Dissecans: Concerning Its Nature and Relation to Formation of Joint Mice, Am. J. Orthop. Surg. **8**:477, 1910-1911.

Freund, E.: Zur Frage der aseptischen Knochennekrose, Virchows Arch. f. path. Anat. **261**:287, 1926.

Friedrich, W.: Ein Fall von Osteochondritis dissecans traumatica, Zentralbl. f. chir. u. mech. Orthop. **7**:401, 1913.

Fritzsche, A.: Die Osteochondritis dissecans, Inaugural Dissertation, Jena, 1890; cited by Neumann, W., and Suter, A.: Deutsche Ztschr. f. Chir. **146**:219, 1918.

Geyman, M. J.: Osteochondritis Dissecans, Radiology **11**:315, 1928.

Grüder: Ein Beitrag zur Entstehung der freien Gelenkkörper durch Osteochondritis dissecans nach König, Deutsche Ztschr. f. Chir. **72**:328, 1904.

Halstead, A. E.: Floating Bodies in Joints, Ann. Surg. **22**:327, 1895.

Harms: Zur Frage der Osteochondritis dissecans am Talus, München. med. Wchnschr. **74**:520, 1927.

——Osteochondritis dissecans an der Talusrolle? Zentralbl. f. Chir. **54**:1017, 1927.

Harris, M. L.: Some Internal Injuries of the Knee Joint, Tr. West. Surg. & Gynec. A., 1901, pp. 50-61.

Hartwich: Beiträge zur Lehre von dem Gelenkmäusen, Arch. f. klin. Chir. **120**: 732, 1922.

Häuptli, O.: Ueber Osteochondritis dissecans, Beitr. z. klin. Chir. **131**:395, 1924.

Heine, J.: Beitrag zur Pathogenese der Osteochondritis dissecans, Deutsche Ztschr. f. Chir. **206**:119, 1927.

Hellström, J.: Beitrag zur Kenntnis der sogenannten Osteochondritis dissecans im Kniegelenk, Acta chir. Scandinav. **55**:190, 1922.

Henderson, M. S.: Osteocartilaginous Joint Bodies, Railway S. J. **25**:49, 1918.

Hildebrand: Experimenteller Beitrag zur Lehre von den freien Gelenkkörpern, Deutsche Ztschr. f. Chir. **42**:292, 1896.

Humphrey, G. M.: Loose Bodies in the Knee-Joint, Brit. M. J. **1**:613, 1888.

Hunter, J.: Some Observations on the Loose Cartilages Found in Joints, and Most Commonly Met With in that of the Knee. The Complete Works of John Hunter, edited by James F. Palmer, Philadelphia, Haswell, Barrington & Haswell, 1841, vol. 3, pp. 583-588.

Journeaux and Hermann, quoted by Wolbach and Allison.

Kappis, M.: Osteochondritis dissecans und traumatische Gelenkmäuse, Deutsche Ztschr. f. Chir. **157**:187, 1920.

——Zur Lehre von den Gelenkmäusen, Deutsche med. Wchnschr. **42**:1161, 1920.

——Ueber Bau, Wachstum und Ursprung der Gelenkmäuse, Deutsche Ztschr. f. Chir. **157**:214, 1920.

——Die anatomische Bedeutung des Wachstums der Gelenkmäuse, Deutsche Ztschr. f. Chir. **170**:367, 1922.

——Tatsachen und Hypothesen in der Erklärung der „spontanen" Entstehung der Gelenkmäuse, München. med. Wchnschr. **69**:1158, 1922.

——Weitere Beiträge zur traumatisch-mechanischen Entstehung der „spontanen" Knorpelablösungen (sogenannten Osteochondritis dissecans), Deutsche Ztschr. f. Chir. **171**:13, 1922.

Kehl: Beitrag zur Frage nach der Ursache der freien Gelenkkörper im Kniegelenk, Arch. f. klin. Chir. **142**:44, 1926.

Klein: Zur Geschichte der Entstehung der Gelenkmäuse, Virchows Arch. f. path. Anat. **29**:190, 1864.

Koch, W.: Ueber embolische Knochennekrosen, Arch. f. klin. Chir. **23**:315, 1879.

König, F.: Ueber freie Körper in den Gelenken, Deutsche Ztschr. f. Chir. **27**:90, 1887.

——Zur Geschichte der Fremdkörper in dem Gelenken, Arch. f. klin. Chir. **59**:49, 1899.

——Zur Frage der Osteochondritis dissecans, Zentralbl. f. Chir. **32**:809, 1905.

——Osteochondritis dissecans (Teilnerkrose an den Gelenkenden), Arch. f. klin. Chir. **142**:600, 1926.

——Diskussionsbemerkung zum Vortrage Fritz König's Osteochondritis dissecans, Arch. f. klin. Chir. **142**:142, 1926.

Konjetzny: Diskussionsbemerkung zum Vorträge Lehmann über Osteochondritis, Zentralbl. f. Chir. **51**:2451, 1924.

Kragelund: Studien über pathologische Anatomie und Pathogenese der Gelenkmäuse, Zentralbl. f. Chir. **14**:412, 1887.

Kroh, F.: Klinische und histologische Beiträge zur Lehre von der Osteochondritis dissecans des Kniegelenkes, Arch. f. klin. Chir. **149**:421, 1928.

Laennec, quoted by Wolbach and Allison.

Läwen, A.: Ueber Osteochondritis dissecans am Talocruralgelenk und ihre operative Behandlung, Zentralbl. f. Chir. **56**:2498, 1929.

Lamas, A.: Osteochondritis Dissecans of the Knee, An. de fac. de med., Montevideo **13**:762, 1928.

——Osteochondritis Dissecans of the Knee: A Case, Rev. de med., Rosario **4**:47, 1929.

Lange, M.: Bilateral Osteochondritis Dissecans of the Head of the Femur, Ztschr. f. orthop. Chir. **51**:269, 1929.

Leb, A.: Die Ätiologie der sogenannten Osteochondritis dissecans (König), Arch. f. klin. Chir. **131**:425, 1924.

Lehmann, J. H.: Ueber Osteochondritis, Zentralbl. f. Chir. **51**:2451, 1924.

——Ist eine Wiedereinheilung osteochondritischer Gelenkmäuse möglich? Deutsche Ztschr. f. Chir. **192**:88, 1925.

——Osteochondritische Gelenkmäuse, Arch. f. klin. Chir. **142**:36, 1926.

Lieck, quoted by Leb.

Linde, F.: Reintraumatisch, infolge von Knebeln entstandenes Corpus mobile, welches das Phänomen des „schnappenden Knies" erzeugt, Zentralbl. f. Chir. **49**:741, 1922.

Lindenstein: Osteochondritis dissecans und Gelenkmäuse, Beitr. z. klin. Chir. **51**:503, 1906.

Löhr, W.: Bemerkung zum Vorträge Lehmann über Osteochondritis, Zentralbl. f. Chir. **51**:2454, 1924.

——Ueber Spontanheilung von Osteochondritis genu, Zentralbl. f. Chir. **52**:1193, 1925.

——Diskussionsbemerkung zum Vorträge Fritz König: Osteochondritis dissecans, Arch. f. klin. Chir. **142**:140, 1926.

——Dauererfolge bei der Behandlung der Osteochondritis dissecans (König), Arch. f. klin. Chir. **157**:752, 1929.

——Etiology and Treatment of Osteochondritis Dissecans and Joint Mice, Zentralbl. f. Chir. **56**:2242, 1929.

Ludloff, J.: Osteochondritis dissecans des Kniegelenkes, Zentralbl. f. Chir. **35**: 161, 1908.

Ludloff, K.: Zur Frage der Osteochondritis dissecans am Knie, Arch. f. klin. Chir. **87**:552, 1908.

McCammon, J. W.: Report of a Case of Osteochondritis Dissecans, J. Med. **8**:80, 1927.

Martens, M.: Zur Kenntnis der Gelenkkörper, Deutsche Ztschr. f. Chir. **53**:348, 1899.

Monro, quoted by Wolbach and Allison.

Moreau: L'ostéochondrite disséeante du genou, Arch. franco-belges de chir. **26**: 131, 1923.

Moulonguet, P.: Foreign Bodies in Joints, J. Bone & Joint Surg. **11**:353, 1929.

Müller, W.: Zur Frage der Osteochondritis dissecans, Zentralbl. f. Chir. (suppl.) **30**:158, 1903.

Neumann, W.: Beitrag zur Kenntnis der Osteochondritis dissecans, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **30**:230, 1918.

——Osteochondritis dissecans und freie Gelenkkörper, Fortschr. d. Med. **37**:57, 1920.

——and Suter, A.: Beitrag zur Frage der Osteochondritis dissecans, Deutsche Ztschr. f. Chir. **146**:219, 1918.

Nieuwejaar, L.: To tilfaelder av osteochondritis dissecans, Norsk. mag. f. lægevidensk. **86**:349, 1925.

Nigst, P. F.: Osteochondritis dissecans des Knies im Sinne Ludloffs, Cor.-Bl. f. schweiz. Aerzte **48**:746, 1918.

——Ueber Osteochondritis dissecans, mit besonderer Berücksichtigung des Ludloffschen Krankheitsbildes, München. med. Wchnschr. **66**:1223, 1919.

Nussbaum, A.: Ueber die Gefäss des unteren Femurendes und ihre Beziehungen zur Pathologie, Beitr. z. klin. Chir. **129**:245, 1923.

Paget, J.: On the Production of Some of the Loose Bodies in Joints, St. Barth. Hosp. Rep. **6**:1, 1870.

Pechlin: Quoted by Wolbach and Allison.

Phemister, D. B.: The Causes of and Changes in Loose Bodies Arising from the Articular Surface of the Joint, J. Bone & Joint Surg. **6**:278, 1924.

Polocco, E.: Osteochondritis Dissecans of the Femoral Condyle, Gior. d. r. Accad. di med. di Torino **92**:184, 1929.

Poncet, quoted by Kappis: Deutsche Ztschr. f. Chir. **157**:186, 1920.

Poulet, A., and Vaillard, L.: Contribution à l'étude des corps étrangers osteo-cartilagineux et osseux des articulations, Arch. de physiol. norm. et path. **5**:266, 1885.

Preiser, quoted by Brackett and Hall.

Rainey, quoted by Wolbach and Allison.

Real, R.: Ein Beitrag zur Kenntnis der Gelenkkörper, Deutsche Ztschr. f. Chir. **38**:1, 1894.

Reeder, H. A.: Osteochondritis dissecans, Inaugural Dissertation, Greifswald, 1913, p. 2.

Richards, G. E.: Osteochondritis Dissecans, Am. J. Roentgenol. **19**:278, 1928.

Ridlon, J.: Osteochondritis Dissecans, J. A. M. A. **61**:1777 (Nov. 15) 1913.

Riedel: Einige Gelenkpräparate: Osteochondritis dissecans, Verhandl. d. deutsch. Gesellsch. f. Chir. **19**:399, 1890.

Rieger, H.: Zur Pathogenese von Gelenkmäusen, München. med. Wchnschr. **67**: 719, 1920.

Rimann, H.: Experimenteller Beitrag zur Lehre von der Entstehung der echten, freien Gelenkkörper, Virchows Arch. f. path. Anat. **180**:446, 1905.

Roesner, E.: Zur Frage der „spontanen" Entstehung der Gelenkmäuse, München. med. Wchnschr. **69**:1757, 1922.

——Die Entstehungs-Mechanik der sogenannten Osteochondritis dissecans am Kniegelenk, Beitr. z. klin. Chir. **127**:537, 1922.

Rokitansky: quoted by Wolbach and Allison.

Salmon, M. J.: Osteochondrite disséquante du coude et de l'épaule, Bull. et mém. Soc. anat. de Paris **7**:608, 1923.

Schirmer, A.: Osteochondritis dissecans des Ellenbogengelenkes, Zentralbl. f. Chir. **52**:26, 1925.

——Osteochondritis dissecans des Ellenbogengelenkes, Schweiz. med. Wchnschr. **22**:489, 1925.

Schmidt, A.: Experimentelle Untersuchungen über das Schicksal teilweise ausgelöster Knorpelknochenlappen von der Gelenkfläche des Kniegelenkes, Beitr. z. klin. Chir. **130**:142, 1923-1924.

——Experimentelle Gelenkfrakturen: Zur Frage der Osteochondritis dissecans, Beitr. z. klin. Chir. **132**:129, 1924.

——Zur Entstehung der freien Gelenkkörper, Beitr. z. klin. Chir. **131**:409, 1924.

von Schmieden: Ein Beitrag zur Lehre von den Gelenkmäusen, Arch. f. klin. Chir. **62**:542, 1900.

Schum, H.: Klinische Beiträge zur Kenntnis der freien Gelenkkörper, Beitr. z. klin. Chir. **141**:111, 1927.

Schumm, H. C.: Osteochondritis Dissecans: Case Report, Wisconsin M. J. **27**: 214, 1928.

Sommer, R.: Die Osteochondritis dissecans (König), Beitr. z. klin. Chir. **129**: 1, 1923.

Staffel, E.: Zur Kenntnis Osteochondritis dissecans, Zentralbl. f. Chir. (suppl.) **21**:90, 1894.

Sultan, G.: Etiology of Free Joint Bodies, Zentralbl. f. Chir. **57**:1049, 1930.

Troell, A.: Zur Kenntnis der Entstehung von freien Körpern im Kniegelenk, mit besonderer Rücksicht auf die sogenannten Osteochondritis dissecans, Arch. f. klin. Chir. **105**:399, 1914.

Veit: Zur Frage der Entstehung der Gelenkmäuse, Deutsche Ztschr. f. Chir. **96**: 394, 1908.

Völker, O.: Beitrag zur Frage von der Entstehung der knorpelig-knöchernen Gelenkmäuse, Arch. f. klin. Chir. **37**:732, 1888.

Vollbrecht: Ueber umschriebene Binnenverletzungen des Kniegelenks, Beitr. z. klin. Chir. **21**:216, 1898.

Walter: Ueber die Osteochondritis dissecans und andere verwandte Gelenkerkrankungen, Verhandl. Med. Naturwiss. Gess. in Münster Sitzg. **14**:6, 1926.

Wegener, T.: Ueber die Entstehung der freien Gelenkkörper mit besonderer Berücksichtigung der Osteochondritis dissecans König, Inaugural Dissertation, Leipzig, 1906.

Wehner, E.: Ein corpus mobile innerhalb der Patella, Zentralbl. f. Chir. **48**:33, 1921.

Weil, S.: Ueber doppelseitige, symmetrische Osteochondritis dissecans, Beitr. z. klin. Chir. **78**:403, 1912.

Wolbach, S. B., and Allison, N.: Osteochondritis Dissecans, Arch. Surg. **16**:1177 (June) 1928.

Wrede, L.: Bedeutung des Traumas für die Entstehung freier Gelenkkörper, Inaugural Dissertation, Berlin, 1899.

Ziegner, H.: Zur Entstehung der freien Gelenkkörper, Med. Klin. **13**:1090, 1917.

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# THE CLOSED INTESTINAL LOOP

## III. ASEPTIC END-TO-END INTESTINAL ANASTOMOSIS AND A METHOD FOR MAKING A CLOSED INTESTINAL LOOP SUITABLE FOR PHYSIOLOGIC STUDIES *

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In order to carry on successfully a series of observations on hydrostatic pressure in closed intestinal loops [1] in dogs, as first demonstrated by Whipple and his associates,[2] it was necessary to develop some method whereby such loops could be made accessible while in an essentially normal environment. These loops have been so satisfactory for determinations other than hydrostatic pressure that we believe that the methods employed are worth reporting. We felt that any method devised should fulfil certain requirements. The loop should be wholly within the peritoneal cavity; its circulation should be normal which in turn would probably insure a normal mucosa over an indefinite period of time; its lumen should be accessible in unanesthetized animals for various types of observations; and the surgical technic necessary to accomplish this should be aseptic and within the ability of investigators accustomed to experiments on animals.

The technic devised is one that we now employ in the formation of a jejunal loop, and it differs only in minor detail for loops made at different levels of the small intestine. Dogs were used in all our work. Animals weighing over 15 Kg. are preferable in that they have small intestines of sufficiently large caliber to facilitate an end-to-end anastomosis. This, though not difficult, offers the only immediate technical difficulty which a little practice can readily overcome. Food was with-

* Submitted for publication, Oct. 20, 1930.

* From the Department of Physiology, University of Oregon Medical School.

* This work was aided by a grant from the Committee on Scientific Research, American Medical Association.

1. Burget, G. E.; Martzloff, K.; Suckow, G., and Thornton, R. C. B.: The Closed Intestinal Loop: I. Relation of Intraloop (Jejunum) Pressure to the Clinical Condition of the Animal, Arch. Surg. **21**:829 (Nov.) 1930. II. Observations on Dogs with Jejunal and Ileal Loops with Blood Chemistry Findings, Arch. Int. Med. **47**:593 (April) 1931.

2. Stone, H. B.; Bernheim, B. M., and Whipple, G. H.: Intestinal Obstruction: A Study of the Toxic Factors, Bull. Johns Hopkins Hosp. **23**:159, 1912.

held from an animal for twenty-four hours before operation. One-half grain (32.4 mg.) of morphine sulphate and one one-hundredth grain (0.6 mg.) of atropine sulphate were given hypodermically one-half hour before ether narcosis was induced. The usual tincture of iodine preparation for the skin was employed.

## OPERATIVE TECHNIC

An upper right rectus incision of suitable length (about 8 cm.) is made about 3.5 cm. from the midline. Treitz' ligament is identified and the jejunum traced

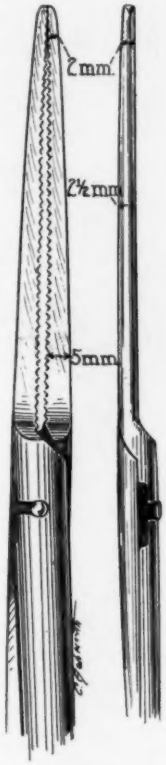


Fig. 1.—Drawing showing clamp with dimensions of the blades. The blades are 9 cm. in length. Note that the blades have some "spring" so that tips come together before the more proximal surfaces. This is done so that when the blades are entirely in contact there will be sufficient pressure at the tips, where the blades are weakest, to prevent the intestine from slipping. The longitudinal groove cannot be seen in this illustration. An ideally constructed clamp of this type should be tongued and grooved longitudinally and without the transverse serrations.

distally. The proximal point at which a jejunal loop can be made and survival anticipated is where the mesenteric veins from the contemplated intestinal segment enter the mesenteric root at right angles. This point varies in its distance from Treitz' ligament and can only be determined in a given animal by examining the

mesenteric root, putting the mesentery under tension and observing the color of the intestine. If one attempts to utilize a segment of jejunum the mesenteric veins of which tend to curve posteriorly as they enter the superior mesenteric vein, the possibility of some circulatory disturbance is considerably increased.

The length of the proposed jejunal loop is dependent on the amount of intestine supplied by a single primary mesenteric artery and vein. Our loops measured from 5 to 12 cm.; a length of 9 cm., however, was a general average. Four clamps are placed on the intestine at either end of the proposed loop. The clamps are applied in such order that the instruments (fig. 2, *C-1* and *C-2*) furthest removed from the end of the loop are placed first. The other clamps are then placed as shown in figure 2. The two most distal clamps are specially designed and will be described. It will be noted that they are placed to form an angle of about 75 degrees with the intestine to which they remain attached for the purpose of later establishing an anastomosis.

The special clamps are simple and inexpensive. It will be noted (fig. 1) that the bite of the clamp is from 2 to 2.5 mm. in width, so that a minimum of trauma-

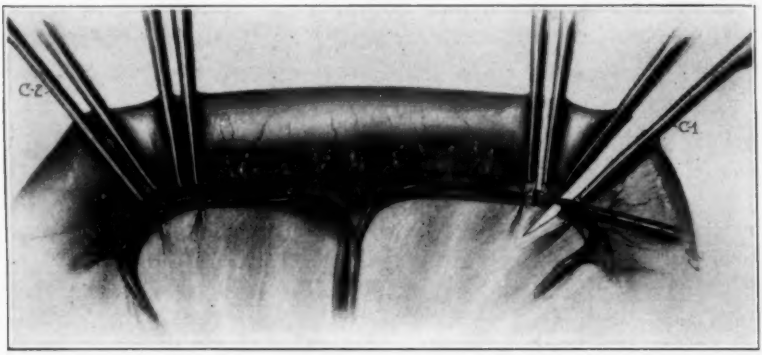


Fig. 2.—Clamps in place preparatory to section of the intestine. The two most distal clamps (*C-1* and *C-2*) are placed to form an angle of less than 90 degrees with the segment of intestine to which they remain attached.

tized tissue is involved in the intestinal anastomosis. One opposing surface is grooved longitudinally and the tips are smooth. More satisfactory, possibly, would be a clamp the opposing surfaces of which were tongued and grooved. For purposes of economy, we did not incur this additional expense. The lips are sufficiently long (9 cm.) to be used on intestine of any diameter and thick enough to insure uniform pressure from tip to base. In our earlier experiments Kocher clamps were used throughout. At times we found them a little short for intestines of larger caliber. The handles were short, so that the assistant's hands were in the way, and the teeth at the tips of the lips were inconvenient when the clamps were removed from the ends of the sutured intestine. The instrument described has overcome these objections.

When the instruments are placed, as shown in figure 2, the vascular arches are ligated and the intestine and mesentery are sectioned with an electrocautery. The ends of the loop are then closed in two tiers with a Parker-Kerr suture of number 00 plain catgut. This suture technic is adequate to withstand a hydrostatic pressure sufficient to rupture the loop at any time after operation. The

loop is then temporarily placed in the peritoneal cavity and the end-to-end anastomosis performed by an aseptic technic.

### ASEPTIC TECHNIC FOR END-TO-END INTESTINAL ANASTOMOSIS

To one familiar with the various methods of aseptic end-to-end intestinal anastomosis, it will be apparent at once that no real originality enters into our method. It is merely a modification of methods previously described.

Without trying to enumerate the various writers who have contributed to the clamp technic of aseptic end-to-end intestinal anastomosis, in contradistinction to the bulkhead method or methods employing special mechanical contrivances such as rubber balloons, rings, cones, etc., we believe that two require special mention. Rostowzew [3] described a technic requiring special and cumbersome clamps which were left on the ends of the divided intestine until the necessary Lembert sutures were in place, when the clamps were removed. The cauterized ends of the intestine remained closed while the previously placed sutures were tied. It should be noted that in Rostowzew's method the ends of the intestine to be united were held not directly end-to-end, but at right angles to the longitudinal axis of the intestine, producing a greater inturning on one side than on the other.

Moszkowicz [4] employed the same technic, with slight mechanical changes, and finally devised a three bladed clamp which, in a far simpler manner, performed the function of the cumbersome instrument first employed by Rostowzew and himself. The technic and instrument described by Rankin [5] nearly twenty years later is in all essential respects the method of Moszkowicz, who was not mentioned by Rankin.

Parker and Kerr [6] described their method of closing both ends of the sectioned intestine by placing "basting stitches" over each of the occluding clamps. These sutures are pulled taut after the clamps are removed and invert the crushed ends of the intestine. The sutures designed to anastomose the two occluded ends of the intestine are then placed and tied, and finally the lumen is reestablished by withdrawal of the previously placed "basting stitches."

All of the clamp methods of aseptic end-to-end anastomosis since described have utilized the features of Rostowzew's operation, as modi-

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3. Rostowzew, M. I.: Aseptische Darmnaht, Arch. f. Chir. **82**:462, 1907.

4. Moszkowicz, L.: Ueber aseptische Darmoperationen, Wien. klin. Wchnschr. **21**:1593, 1908; Ueber aseptische Darmanastomosen, ibid. **22**:848, 1909.

3. Rostowzew, M. I.: Aseptische Darmnaht, Arch. f. klin. Chir. **82**:462, 1907. Gynec. Obst. **47**:78, 1928.

6. Parker, E. M., and Kerr, H. H.: Intestinal Anastomosis Without Open Incisions by Means of Basting Stitches, Bull. Johns Hopkins Hosp. **19**:132, 1908.

fied by Mosckowicz, while some have utilized the principles of the Parker-Kerr method.

Pringle [7] and Scarff [8] eliminated in their methods the angulation of the ends of the intestine, which is the basic objection to the Rostowzew-Moskowicz operation, by bringing them into direct apposition. This eliminates the turning in of intestinal spurs of unequal length and also the carrying of sutures across the end of cauterized intestine. However, in both technics mattress sutures are inserted while the clamps are still in place. In our experience, this procedure makes it difficult to place the mattress sutures accurately; occasionally opposite walls of the intestine are sutured together. In order, then, to reestablish the intestinal lumen at the line of anastomosis, the occluding suture must be removed with a resultant break in asepsis.

The advantages that we have experienced in our modified technic as compared with the others that we have used are: 1. A minimal amount of tissue (from 2 to 2.5 mm.) is devitalized with the instrument described. 2. The first row of Parker-Kerr sutures does not cross the end of cauterized intestine and is placed so close to the clamps that it adds about an additional millimeter to the inturned flange. 3. The ends of the Parker-Kerr sutures, when tied, allow ready manipulation of the intestine with minimal trauma and the accurate placing of mattress sutures. In the forty-one dogs and two patients on whom this identical technic was used, the intestine was not transfixed, healing was uneventful, except as noted, and obstruction at the site of anastomosis occurred in one dog.

Leakage at or near the site of anastomosis occurred in three animals: (1) in a duodenal anastomosis in which the ends of intestine were brought together under tension and a round worm was burrowing through at the suture line; (2) in an anastomosis in which the intestine distal to the line of suture was plugged with worms and a worm was coming through the line of anastomosis, and (3) about 1 cm. proximal to the line of suture in a dog that died, as did the other two, of a peritonitis secondary to the rupture of the intestinal loop.

In eight other dogs not included in the previously noted forty-one, we used number 0 catgut for our Parker-Kerr basting stitches and found leakage in two, so the use of catgut was abandoned.

Obstruction at the site of anastomosis occurred in one animal (no. 91) which lived for six weeks. This was due to a thick adhesion on one side of the anastomosis which prevented the inturned flange from unfolding as it had on the opposite side. It should be remembered that in

7. Pringle, S.: Aseptic Resection of the Intestine, Brit. J. Surg. **12**:238, 1924.

8. Scarff, J. E.: Aseptic End-to-End Suture of the Intestine, Ann. Surg. **83**:490, 1926.

many of our animals a peritonitis of varying duration occurred, owing to damage to the closed intestinal loops, so that the intestinal anastomoses were often exposed to surroundings that favored infection, inflammation and adhesions.

We used the technic described by Scarff in forty-seven dogs. A leak, not caused by worms, developed at the site of suture in eight, so we adopted the method described here.

The anatomic details of our operative results will be given in another paper. The technic employed by us is as follows:

*Technic.*—The two special clamps are brought together and rotated in their longitudinal axes so that their uneven surfaces are face to face. A continuous

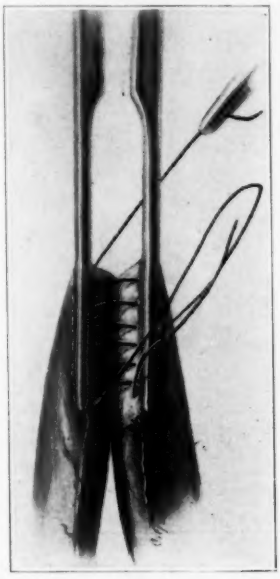

Fig. 3.—Specially designed clamps rotated in their longitudinal axes so that the first Parker-Kerr suture can be placed.

right-angled serosubmucosal suture of number 0 black silk on a curved intestinal needle is placed in the two opposing intestinal walls as close to the clamps as possible (fig. 3). The sutures should begin on the antimesenteric margin of one intestinal segment and terminate on the mesenteric border. The free ends are secured, the clamps are rolled so that their even surfaces are opposed and a similar suture is placed so that it begins and terminates on sides of the clamps opposite to its counterpart, as shown in figure 4.

The anastomosis clamps are now removed, one at a time, while both ends of the sutures are held slightly taut (fig. 5). When the last clamp is off, the sutures are pulled tightly and tied snugly enough to narrow the diameter of the anastomosis by 1 or 2 mm. (fig. 6) in order to invert the crushed intestine at both the mesenteric and the antimesenteric margins. During this manipulation the cauter-

ized end of the gut does not open when the clamp described is used, and no difficulty is experienced with the mesenteric aspect of the intestine.

The ends of the previously placed sutures now serve as stay sutures with which the intestine can be rotated in its longitudinal axis. The first line of sutures is now reenforced by a second row of closely placed Halsted mattress stitches of 0 black silk on milliner's needles (fig. 7). At first we left one long suture on opposite sides of the anastomosis in order to apply traction and thereby assure the patency of the lumen. This was done because with Scarff's technic it occasionally happened that one or two sutures penetrated to the opposite intestinal wall, thereby closing the lumen. This necessitated the removal of the faulty stitches with consequent breach of asepsis. With the present method the foregoing has never occurred. We have abandoned the use of these accessory traction

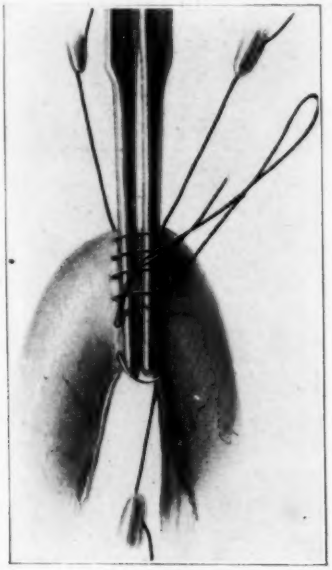

Fig. 4.—The clamps have been rotated so that their flat surfaces are in apposition and the second Parker-Kerr suture is being placed.

sutures and never invert the intestine through the anastomatic lumen to insure its patency. The mesenteric defect is closed with interrupted fine black silk sutures.

*Method of Fixing the Loop.*—The loop is again brought out of the peritoneal cavity and laid over the lateral margin of the incision. Allis clamps are placed on the peritoneum of the medial aspect of the incision, traction is exerted and the midline fatty appendage is dissected medially to the linea alba the length of the incision. This denuded area is further traumatized by rubbing it with dry gauze.

The middle two thirds to three fourths of the loop is sutured (figs. 8 and 9) as closely as possible to the right of the linea alba with number 0 interrupted black silk on curved intestinal needles, care being taken not to penetrate the submucosa too deeply, to prevent subsequent rupture of the loop at the point of suture. It is preferable to err on the side of safety and suture only the intestinal muscularis. In our experience, all loops so attached have adhered to the anterior abdominal wall.

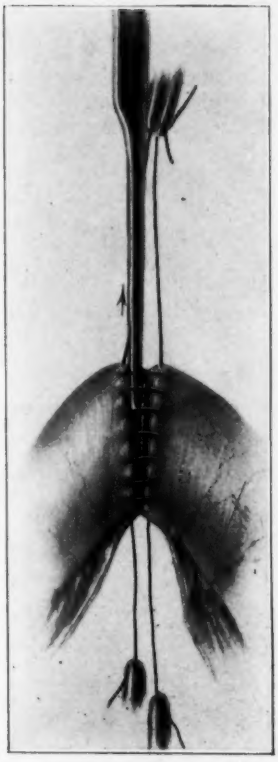

Fig. 5.—The last clamp is being withdrawn leaving two narrow segments of crushed intestine in direct apposition. The sutures are placed closer to the crushed end of the intestine than the illustration shows.

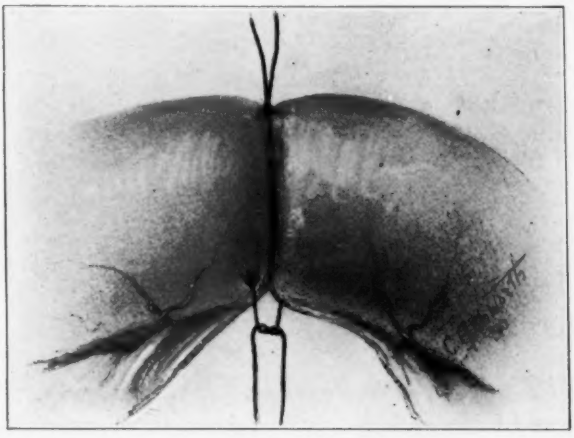

Fig. 6.—The two Parker-Kerr sutures have been drawn taut and tied. The cauterized ends of the intestine remain closed during the entire procedure.

A guide of linen is next placed in the skin of the anterior abdominal wall to the left of the midline at a level where the loop can be reached by a hollow needle passed through the abdominal wall just to the right of the linea alba.

The wound is closed with catgut and heavy linen and no dressing is applied. The dog is given water after the third day and milk and hamburger steak on the fifth day. Skin sutures are removed on the fifth day.

### CARE OF ANIMAL AFTER OPERATION

As essential to the survival of the animal as the proper operative technic is the postoperative care of the closed loop. It should be tapped just to the right of the midline at a point opposite the linen guide suture under aseptic precaution with a number 19 needle on a syringe, from eighteen to twenty-four hours after operation and every twenty-four hours thereafter until no further secretion is obtained. Aspiration is facilitated by the postoperative anesthesia of the abdominal wall between

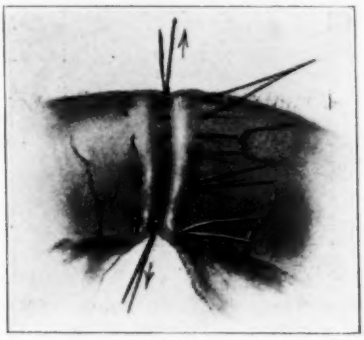

Fig. 7.—Halsted mattress sutures of fine black silk on milliner's needles are used to complete the anastomosis. The sutures are placed somewhat more closely than is depicted in the illustration and need not be "reenforced," for this suture line is adequate when properly placed.

the incision and the linea alba. This lasts for months and the animals are entirely docile while being manipulated. It is advantageous after aspiration of the contents of the loop to wash the loop with physiologic solution of sodium chloride. We believe that this hastens restoration of the loop to normal by removing the inflammatory products incident to the operative trauma.

There is considerable variation in the behavior of the loops. After three or four aspirations and washings some may go for varying periods before this again becomes necessary.

When loops are made lower in the small intestine, aspiration need not be instituted so soon after operation. Provided the loop is one that survives and will be suitable for various types of observation, this may be commenced when the sutured ends have sloughed and healed over,

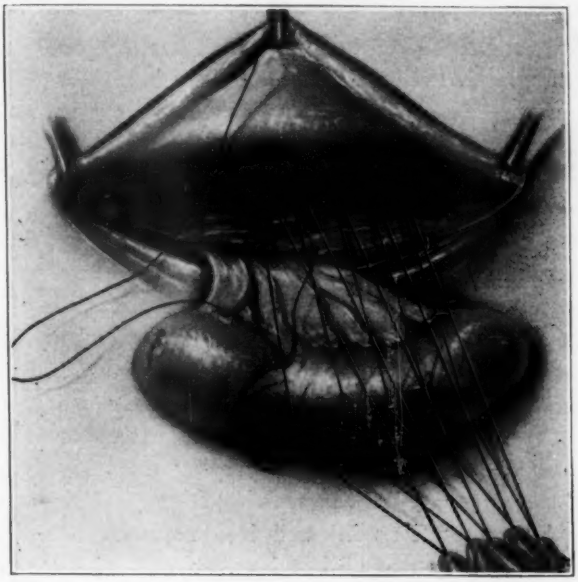

Fig. 8.—Sutures are placed but not tied.

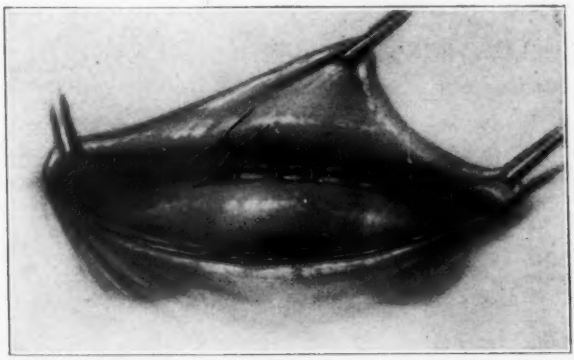

Fig. 9.—Loop sutured in place. Sutures are carried sufficiently near to the ends to prevent bagging when the loop is being aspirated.

which requires a period of from ten to fourteen days. As previously noted, various loops, even though destined to survive, require aspiration at various intervals. In the case of loops that have not become distended for some time, our first clue that the animal has a distended loop is its loss of appetite, lack of animation and increase in temperature. Almost immediately after the intraloop pressure is relieved, the animal is spirited and will take food.

When one desires to use a loop that has not been aspirated for some time for studies of digestion or absorption, it is necessary to aspirate and wash the loop a day or two previously in order to free it from the epithelial and bacterial residue. In old loops that have not been disturbed for several weeks there is a gradual accumulation of a grayish, putty-like material which, after several months, will entirely fill the loop.

This procedure was carried out on ninety-two dogs. Some of the animals lived for months, in one instance for over one year, without aspiration of the loop except for a few days after operation; others, again, had to be aspirated at intervals varying from days or weeks, to months, and some of these have been living for a year or more.

We found that solutions injected into these closed loops can be aspirated so successfully that all but 1 cc. or a fraction thereof can be recovered.

Over a period of about a year animals with closed intestinal loops were subjected to various determinations of blood chemistry, the loop contents were studied bacteriologically, and observations on digestion and absorption were made with cane sugar, levulose, fats and peptones.

### VALUE FOR PHYSIOLOGIC INVESTIGATION

It is evident, we believe, that this type of loop presents unusual possibilities for various types of observations, in that it overcomes some of the shortcomings present in the other experimental methods. As compared with the intestinal loop lying in the peritoneal cavity of anesthetized and decerebrate animals, our method has the advantage of not being an acute experiment under anesthesia while our determinations are not made on recently traumatized intestine. This method also overcomes the objection inherent in the use of closed surviving intestinal segments suspended in Tyrode's or Locke's solution in that our loops are viable, in a normal environment, and can be used repeatedly.

The Thiry-Vella fistula technic and the polyfistula method of London[9] have definite shortcomings in that they produce fistulas, subject to secondary infection and abnormal exposure to atmospheric pressure.

9. London, E. S., in Abderhalden: Handbuch der biologischen Arbeitsmethoden, Vienna, Urban & Schwarzenberg, 1926, vol. 6, pp. 491 and 544.

They also present the factor of error due to difficulty in recovering *in toto* the remains of injected solutions; the polyfistula method brings in an additional phenomenon of motor function, which is undesirable for some determinations. The method devised obviates, either altogether or in a large measure, the foregoing experimental difficulties in that it provides a fixed and accessible closed loop in a normal environment which affords a histologically normal mucosa in a fairly large percentage of animals. Finally the unabsorbed residue of solution injected into such a loop is recoverable to within approximately 1 cc. of its total volume. During experiments on the digestion of levulose we have also performed laparotomy and aspirated blood from the mesenteric vein of the loop for simultaneous comparison with the heart's blood. These and other observations are being prepared for publication.

# SCALENIOTOMY IN THE SURGICAL TREATMENT OF PULMONARY TUBERCULOSIS *

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In 1822 Carson [1] sounded the keynote to the surgical treatment of pulmonary tuberculosis when he said, "It has long been my opinion that if ever this disease is to be cured, and it is an event of which I am by no means disposed to despair, it must be accomplished by mechanical means, or in other words by a surgical operation." There have since been evolved, roughly speaking, two types of operative procedure in these cases. The first type includes extrapleural paravertebral thoracoplasty suggested by Brauer [2] and performed by Friedrich in 1907, in which they advocated an extremely radical operation which carried with it a high mortality. However, the technic was soon modified by Wilms [3] and Sauerbruch,[4] but even to the present time it continues to carry many disappointing results, both in the immediate effects and later in the resultant spread of the disease in the contralateral lung.

In the second type are classed several conservative procedures, including artificial pneumothorax, first instituted by Potain [5] in 1880. Artificial pneumothorax will not be considered in this report. Extrapleural pneumolysis was performed by Tuffier [6] in 1883, phrenicotomy

* Submitted for publication, Sept. 25, 1930.

* From the Departments of Surgery and Medicine, University of Wisconsin Medical School.

1. Carson, J., cited by Riviere in Essays Physiological and Practical, Liverpool, F. B. Wright, 1822.

2. Brauer, L.: Erfahrungen und Ueberlegungen zur Lungenkollapstherapie. Die ausgedehnte extrapleurale Thorakoplastik, Beitr. z. Klin. d. Tuberk. **12**:49, 1909.

3. Wilms, M.: Die Pfeilerresektion der Rippen zur Verengerung des Thorax bei Lungentuberkulose, Therap. d. Gegenw. **54**:17, 1913.

4. Sauerbruch, F., and Ehring, H.: Die extrapleurale Thorakoplastik, Ergebn. d. inn. Med. u. Kinderh. **10**:869, 1913.

5. Potain: Des injections intrapleurales de l'air stérilisé dans le traitement des épanchements pleuraux consécutifs au pneumothorax, Bull. Acad. de méd. **19**:537, 1888.

6. Tuffier, T., cited by Alexander in L'Etat actuel de la chirurgie intrathoracique, Paris, Masson et Cie, 1914, pp. 90-105; 163-172.

by Stuertz [7] in 1911 and by Felix [8] in 1922, intrapleural pneumolysis by Jacobaeus [9] in 1913, and multiple intercostal neurectomy was introduced by Alexander [10] in 1929. Of these, phrenicotomy is the most frequently used, and it is the simplest of the operative procedures. It is attended by a low rate of mortality, and until recently has been used merely as an adjunct to paravertebral thoracoplasty. Of late, however, this procedure has been proved by Matson [11] to have a marked therapeutic value of its own in the arrest of pulmonary tuberculosis, in addition to its adjunctive or test value. Up to the present when phrenicotomy as an independent procedure has been considered inadequate no recourse has been available other than the most radical type of operation, namely, paravertebral thoracoplasty. Therefore it seemed logical to seek some means of enhancing the value of phrenicotomy in order to produce the arrest of the disease without relinquishing the more conservative procedures.

Intercostal neurectomy and phrenic block are operative through the interruption of the motor nerves to important muscles of respiration. For an understanding of the rationale of such procedures, it is necessary to comprehend the contribution of these muscles to the mechanics of respiration. In his convincing clinical and experimental studies, Hoover [12] assigned certain definite values to the scaleni, the intercostal muscles and the diaphragm in respiration. Briefly stated, this observer concluded that the scaleni anchor the first ribs for the action of the upper three intercostal groups. Through their influence the intercostal muscles tend to bring about a bucket-handle movement of these ribs. The net result of this action is to induce an increase in the lateral and the anteroposterior dimensions of the thorax; but, if unopposed, such

7. Stuertz: Künstliche Zwerchfellähmung bei schweren chronischen einseitigen Lungenerkrankungen, Deutsche med. Wchnschr. **37**:2224, 1911.

8. Felix, W.: Anatomische, experimentelle und klinische Untersuchungen über den Phrenikus und über die Zwerchfellinnervation, Deutsche Ztschr. f. Chir. **171**:283, 1922.

9. Jacobaeus, H.: Endopleurale Operationen unter der Leitung des Torakoskops, Beitr. z. Klin. d. Tuberk. **35**:1, 1916.

10. Alexander, J.: Multiple Intercostal Neurectomy for Pulmonary Tuberculosis, Am. Rev. Tuberc. **20**:637, 1929.

11. Matson, R. W.: Exairesis of the Phrenic Nerve in the Treatment of Pulmonary Tuberculosis, Am. Rev. Tuberc. **22**:1, 1930.

12. Hoover, C. F.: The Functions of the Diaphragm and Their Diagnostic Significance, Arch. Int. Med. **12**:214 (July) 1913; Diagnostic Signs from the Scaleni, Intercostal Muscles and the Diaphragm in Lung Ventilation, Arch. Int. Med. **20**:701 (Nov.) 1917; The Functions and Integration of the Intercostal Muscles, Arch. Int. Med. **30**:1 (July) 1922; Respiratory Excursion of the Thorax, Oxford Medicine, New York, Oxford University Press, 1918, vol. 2, p. 29.

a function would result in the shortening of the longitudinal axis of the thorax. Accordingly, the pistonlike descent of the diaphragm on inspiration preserves this longitudinal dimension. Further important clinical observations were made by Hoover on the movements of the costal margin, normally and under pathologic conditions. For the present purposes these may be summarized briefly in the statement that normally the movement of the costal borders on inspiration is slightly outward. The diaphragm tends to pull the costal margins inward, and the antagonism of the scaleni and the intercostal muscles is expressed in their outward, upward pull. The scalene-intercostal group of muscles is more advantageously placed from a mechanical standpoint, and the resultant force represents the algebraic sum of the two in a slight outward movement of the costal margins on normal inspiration. As Hoover emphasized, variations in the undulatory movements of the upper ribs and in the excursions of the costal margins afford valuable diagnostic information as to underlying pathologic conditions.

Abundant evidence has accumulated to render judgment in the case of phrenic block, temporary or permanent. The logic of intercostal neurectomy would seem well grounded. From an anatomicophysiologic standpoint, it has seemed remarkable that the important scalene group should have escaped surgical attention.[13] Certainly Hoover [14] gave ample evidence of their mechanical importance. By clinical cases and experimental division of the scaleni, he was able to demonstrate a caudad movement of the unsupported first rib on inspiration, together with the manubrium, the second and the third ribs. Under such conditions, the fourth rib remained stationary, and not until the fifth rib was reached did the customary undulatory movement appear. From this level downward, the normal bucket-handle movement was exaggerated. Two children with cervical Potts' disease leading to paralysis of the scaleni have been studied in the Wisconsin General Hospital. In both of the patients the classic picture afforded by Hoover was confirmed. The most striking features were the caudad movement of the upper three ribs and the exaggerated outward movement of the costal margins on inspiration. Fluoroscopic examination established the motility of the

13. In qualification of this statement, attention is directed to the suggestion of Coffey (Northwest Med. **28**:108 [March] 1929) that division of the scalenus anticus and medius affords a most advantageous approach for resection of the anterior arc of the first rib, and to that of Grégoire (Paris méd. **1**:265, 1930) which utilizes scalene section as an adjunct to apical extrapleural pneumolysis. Neither of these observers has been interested in the essential motor phenomena of scalene activation.

14. Hoover (footnote 12, second, third and fourth references).

diaphragm in both of these subjects, although the sharp outward movement of the costal margins had led to a suspicion of an associated phrenic paralysis. Hoover further observed that in quiet inspiration the scaleni do not elevate the first ribs, but by their tone they neutralize the caudad tendency of intercostal contraction in this location. In one of his clinical patients [15] in whom intercostal paralysis had occurred, the scaleni were capable of inducing a cephalad movement of the sternum and first upper pair of ribs on quiet as well as deep inspiration. On forced inspiration this subject could increase the circumference of the thorax ¾ inch (19.05 mm.) at the third and at the sixth interspaces through scalene action. From these observations, the scaleni would seem to afford an unusually advantageous point of attack for immobilization of the pulmonary apexes.

The scaleni are three (rarely four) muscles of the deep cervical group. They arise from portions of the transverse processes of the third, fourth, fifth, sixth and seventh cervical vertebrae and insert by tendinous bands into the first and second ribs. Their origins are concealed by the sternocleidomastoid muscle, but their insertions are more widely separated. The largest and longest of these muscles is the scalenus medius, followed in order by the anticus and posticus. The scalenus anticus inserts into the scalene tubercle on the upper surface of the first rib. Rarely, this insertion is split by the subclavian artery, and two distinct muscles are formed. The lateral muscle is then known as the minimus. The scalenus medius inserts into the upper surface of the first rib at about a centimeter posterior to the insertion of the anticus. Some fibers may extend forward and insert into the upper edge of the second rib. The scalenus posticus inserts into the outer surface of the second rib. The nerve supply to these muscles is derived from the cervical plexus, and the posticus may receive branches from the brachial plexus.

The surgical approach used for the division of these muscles is somewhat similar to the one employed in the approach through the subclavian triangle of the neck for exposure of the phrenic nerve. Owing to the origin of these muscles through numerous tendinous slips from the transverse processes of the lower cervical vertebrae, approach at this point is necessarily rendered difficult and inadvisable. The points of insertion into the first and second ribs, however, are through tendons that are easily identified when the other structures are carefully retracted. It is because of their accessibility at this point that the section of each muscle is made near its insertion.

15. Hoover (footnote 12, fourth reference).

TECHNIC

The patient is given a preliminary dose of 1/6 grain (0.01 Gm.) of morphine sulphate and 1/150 grain (0.0004 Gm.) of scopolamine two hours before operation. The same dosage is repeated one hour later or one hour before operation. The position on the operating table is important to effect the best exposure. The patient is placed in the supine position, with his head turned as far as possible to the side opposite to the operative field. Sand bags or other measures to elevate

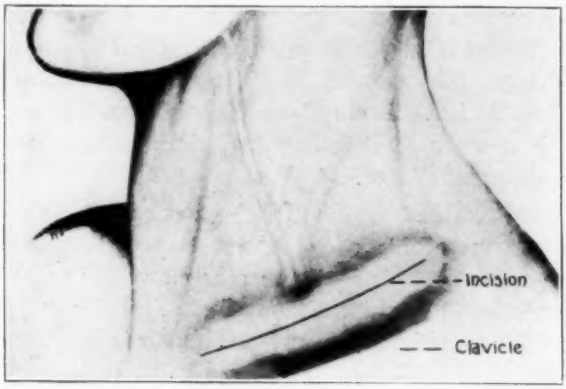


Fig. 1.—The illustration shows line of incision infiltrated with procaine hydrochloride anesthesia. Note the line of the incision about 1.5 cm. above the clavicle.

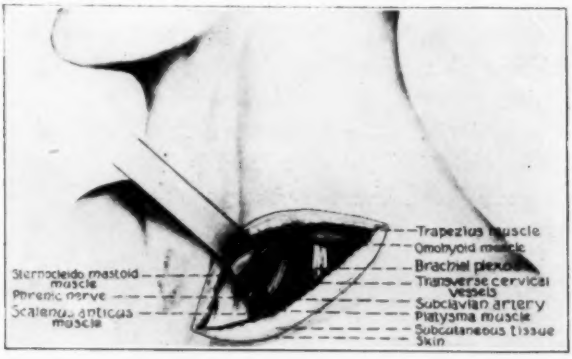


Fig. 2.—The illustration shows the scalenus anticus muscle with the overlying phrenic nerve exposed by retraction forward of the posterior belly of the sternocleidomastoid muscle.

the head or shoulder are inadvisable, since such manipulations tend to relax the scaleni. Rotation of the head to the opposite side, however, has two distinct advantages in that the sternocleidomastoid muscle is thrown forward, and the scaleni are placed under tension. The operative field is thoroughly prepared and draped. A 0.5 per cent solution of procaine hydrochloride is used. A wheal, extending from the posterior edge of the sternocleidomastoid muscle about 1.5 cm. above the clavicle backward to the anterior edge of the trapezius muscle, is

raised in the skin. The subcutaneous tissue and platysma muscle are thoroughly infiltrated, care being taken not to inject any of the solution into the external jugular vein that crosses the line of incision. This procedure requires from about 15 to 20 cc. of the solution. After five minutes the incision in the skin is made along the line of infiltration, following one of the skin folds. Little bleeding occurs on incision of the skin and superficial layers. The deep cervical fascia is then carefully divided, exposing the fatty tissue which is rich in blood supply. By careful blunt dissection the inferior belly of the omohyoid muscle is brought

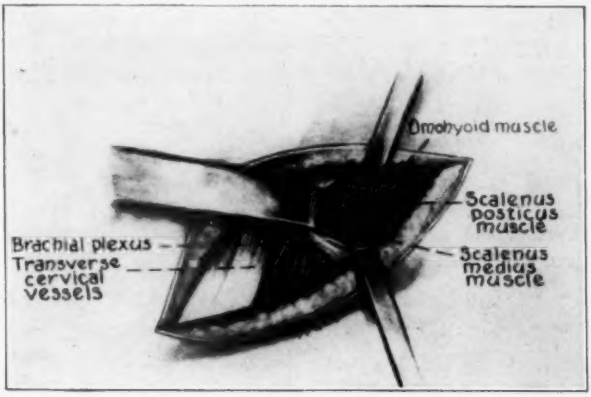


Fig. 3.—The brachial plexus retracted forward, the omohyoid muscle upward and the transverse cervical vessels downward, exposing the scalenus medius and the scalenus posticus muscles.

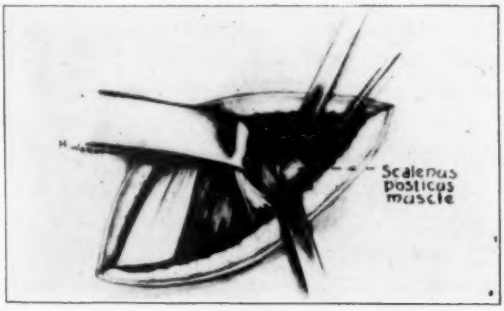


Fig. 4.—Same exposure as figure 3, showing the scalenus posticus muscle ready for division.

into view. This muscle serves as a useful landmark; the anterior portion, as it passes beneath the sternocleidomastoid muscle, overlies the scalenus anticus, which can be well demonstrated at this point by having the patient attempt to lift his head from the pillow. This movement brings all of the scaleni into relief by increasing their tension. Just above the point of crossing the sternocleidomastoid and the omohyoid muscles, the phrenic nerve will be seen on the anterior surface of the scalenus anticus directly beneath the muscle sheath. This also serves as a further useful landmark. About 1 cm. posterior to the insertion of the scalenus

anticus will be found the insertion of the larger scalenus medius. Lying between these muscles close to the first rib is the subclavian artery. The scalenus posticus is in close apposition to the medius, and it is not always possible to identify positively each as a separate muscle.

In exposing these muscles, care must be taken not to injure the brachial plexus or the transverse cervical vessels. By careful retraction this can be done without pain to the patient. When all the insertions are located, each muscle is infiltrated with a small amount of the procaine hydrochloride solution. They are then gradually separated from the surrounding structures until a straight aneurysm needle can be hooked beneath them. For dividing the muscles, the cautery knife is superior to the scalpel. Because of the coagulating effect of the former, there is little or no bleeding. During the division of the several scaleni, all important adjacent structures must be protected. Following their division, the field is carefully inspected for hemostasis, and the deeper layers are then closed by interrupted sutures of 0 plain catgut in the platysma muscle. The skin is sutured with a running subcuticular stitch, which is removed on the fifth day leaving an inconspicuous hair line scar. If the field is not entirely dry, a small rubber drain may be inserted, so that the excessive oozing of serum and blood will not collect beneath the skin. This drain should be removed after the first twenty-four hours.

## INDICATIONS FOR OPERATION

The indications heretofore given for phrenic block have been numerous and diversified, but the results obtained depend on certain anatomicophysiologic alterations occurring within the thorax. At first it was thought that paralysis with subsequent rise of the diaphragm would benefit only basal lesions through compression. Time has proved this idea fallacious, because far removed lesions throughout the lung are benefited. This would not be true if the paralysis and the rise of the diaphragm induced merely compression phenomena. There is also a relaxation of the lung with a resultant contraction. The vital capacity is temporarily lowered, but this is soon compensated largely by the opposite lung. The other important muscles of respiration continue to function, and in these persons there is increased intercostal and scalene activity. The chief therapeutic effect is realized through the diminution in the size of the thorax in the longitudinal axis and in the relaxation of the affected lung. Further evidence of these circumstances is manifest by results which show that the degree of improvement is in direct proportion to the extent of rise of the paralyzed diaphragm. In the cases in which this rise is limited by complicating costophrenic adhesions, the results have been disappointing in the main. Rest is an enemy of tuberculosis, and when beneficial results have been produced by therapeutic measures where this is not the chief factor, its addition should enhance their value. It seems especially important that the remote apical lesions due to previously mentioned respiratory phenomena should be benefited by this adjunct. The performance of simultaneous scaleniotomy and phrenic block seems from anatomico-

physiologic considerations to be a logical procedure which does not depart in principle from the more conservative operations, namely, phrenic block and intercostal neurectomy. If phrenic block is carried out simultaneously with scaleniotomy, it is better to delay the former to the end of the combined operation to avoid the pain resultant from the evulsion of the nerve.

Up to date, in seven cases, patients have been subjected to scaleniotomy. In the first two cases, phrenic block was followed by scaleniotomy one week later. In the remaining five cases a combined operation was done. In every case there was a marked reduction in the respiratory excursion of the upper portion of the thorax. The caudad movement of the upper three ribs, which was recorded by Hoover on scalene paralysis or experimental section, has not been seen in any of these seven patients. An important observation in the five instances of combined scaleniotomy and phrenic exeresis was the constant absence of the increased upper intercostal movement, so commonly seen when the phrenic nerve alone is blocked or evulsed.

These patients showed very little reaction following operation, and suffered little or no discomfort, except for a slight temporary stiffness of the neck with some limitation of motion owing to pain during the first twenty-four hours. This was not severe enough to necessitate a sedative. In one case a hematoma developed forty-eight hours after operation. This complication has not occurred since the cautery has been used for division of the muscles. There has been no resultant sign of deformity or permanent restriction of motion of the head and neck. In the cases in which the operation was done in two stages, scaleniotomy following phrenic block, the vital capacity showed a decrease of from 8 to 9 per cent after scalene section. In one instance following scaleniotomy, the fever which previously had been continuously remittent, after the third day fell to normal, with a decrease in the sputum and marked subjective improvement. In the remaining cases the patients have not been under observation over a sufficient period of time to warrant final conclusions.

## CONCLUSIONS

1. Phrenic block has an established place in the surgical treatment for pulmonary tuberculosis, regardless of location. This measure may be useful either independently or as an adjunct to thoracoplasty. The utilization of phrenic block as a test of the patient's recuperative power or resistance is a recognized procedure.

2. The increased respiratory activity of the upper part of the thorax after paralysis of the diaphragm raises a question as to the physiologic soundness of the operation in apical lesions.

3. From experimental and clinical studies the scaleni have been proved to have an important relation to the respiratory activity of the upper part of the thorax.

4. In a series of cases of pulmonary tuberculosis scaleniotomy has induced satisfactory immobilization of the involved apex.

5. Combined scaleniotomy and phrenic block apparently answer the need for some surgical measure to induce apical rest coincident with paralysis of the diaphragm. When phrenic block has not effected the desired improvement, scaleniotomy may be performed as an adjunct of a conservative type at a later period, before resorting to a radical measure.

6. The anatomic relationships render simple the combined operation (scaleniotomy and phrenic exeresis).

7. Alone or combined with phrenic exeresis, scaleniotomy must be considered as a preparatory stage when more radical measures are inevitable.

8. Through section of the scaleni, the first rib is subjected to the caudal pull of the intercostal muscles; therefore, when paravertebral thoracoplasty must subsequently be performed, the extent of the resection of the first rib may be reduced and the desired effect obtained. Hence the technical difficulties in the surgical approach to this portion of the first stage of the thoracoplasty may be materially reduced.[16]

16. Since the manuscript of this paper was submitted, two articles have appeared in the continental literature closely paralleling our work and results, namely: H. Els (Zentralbl. f. Chir. **57**:2228 [Sept. 6] 1930) and Koch, Els and Junkersdorf (Beitr. z. Klin. d. Tuberk. **75**:772 [Oct. 3] 1930).

# ACUTE PANCREATITIS (PANCREATIC NECROSIS)

## AN EXPERIMENTAL AND CLINICAL STUDY, WITH SPECIAL REFERENCE TO THE SIGNIFICANCE OF THE BILIARY TRACT FACTOR *

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MINNEAPOLIS

The consistent frequency with which gallstones or disease of the gallbladder have been found in association with acute pancreatitis has served to confirm the belief that biliary infection predisposes to pancreatitis. Fitz, who recognized acute pancreatitis as a disease entity, was cognizant of a probable causative relationship between disease of the gallbladder and pancreatitis.

In 1907, Egdahl found that gallstones were present in 42 per cent of 107 reported cases. In a recent statistical study, Schmieden and Sebening found that gallstones were present in 69.8 per cent of a series of 1,278 cases of acute pancreatitis collected from 104 German surgical clinics, from 1919 to 1927. That disease may be present in the gallbladder in the absence of gallstones in no small number of cases is evidenced by the number of instances in which cholecystectomy is performed in the absence of cholelithiasis. In 1919, W. J. Mayo stated that infected gallbladders and usually stones were present in 90 per cent of all cases of acute and chronic diseases of the pancreas in which operation was performed at the Mayo Clinic. It is significant, too, that in Schmieden and Sebening's report, 65 per cent of the total number of instances of acute pancreatitis occurred in women, whereas a number of previous smaller statistical studies have shown a predominance in men. The latter observation is in agreement with the greater incidence of disease of the gallbladder in women.

The importance of this frequent association is further emphasized by the fact that two commonly discussed etiologic factors of acute pancreatitis seek their explanation in a coexisting disease of the biliary

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* Acute pancreatitis and acute pancreatic necrosis have been used interchangeably in this paper. The term pancreatitis is so well established in the literature that it would appear futile to substitute the more accurately descriptive designation of pancreatic necrosis.

tract. The acceptance of the reflux of bile as an etiologic agent in acute pancreatitis centers about the observation of Opie that a gallstone lodged at the ampulla of Vater may convert the choledochus and duct of Wirsung into a common channel and permit the retrojection of bile into the pancreatic duct. Since Opie's report in 1901, a large number of similar observations have been recorded. The experimental production of acute pancreatitis by the injection of bile into the pancreatic duct by many investigators has served to confirm the significance of Opie's observation.

Serious consideration of the lymphatic factor as an etiologic agent of acute pancreatitis dates from the experimental work of Maugeret in 1908. Though failing to effect an acute pancreatitis by producing a chemical cholecystitis in the dog following the introduction of formaldehyde and charcoal into the gallbladder, Maugeret believed that the swelling and interstitial edema of the gland demonstrated that infection may be propagated to the pancreas from the biliary passages by the lymphatic route.

This suggestion soon found corroboration in the clinical observations of Arnsberger, viz., that evidence of pancreatic injury may obtain in acute infections of the biliary tract. In this country, Deaver in particular has championed the belief that acute pancreatitis results through the spread of infection from the gallbladder to the pancreas by way of the lymphatics. Now, it is endorsed by many, and appears to have found substantial support in the experiments of Graham and Peterman.

Recently, however, Kaufmann [1] stated that no experimental or clinical proof exists for the origin of acute pancreatitis through the medium of lymphangitis extending from infection in the gallbladder. In their monograph on "Diseases of the Gall Bladder and Bile Ducts" (1928), Graham and his associates stated that "we were probably in error in our former conclusion that we had demonstrated a lymphogenous origin of pancreatitis from a cholecystitis." The virtual abandonment of the bile factor as an etiologic agent in the genesis of acute pancreatitis by Mann and Giordano [2] has dealt a severe blow to the other factor that made special recognition of a causative relation between the frequent association of disease of the gallbladder and acute pancreatitis.

Clinically, the common factor or denominator (at least, far more frequent than any other single factor) of acute pancreatitis is disease of the biliary tract. For a long time, this fact has been recognized.

1. Kaufmann, M.: Surg. Gynec. Obst. **44**:15, 1927.

2. Mann, F. C., and Giordano, A. G.: Bile Factor in Pancreatitis, Arch. Surg. **6**:1 (Jan.) 1923.

The mechanism through which disease of the gallbladder predisposes to pancreatitis has been in dispute. The denial of the existence of experimental proof for the genesis of pancreatitis through the reflux route as well as through a lymphatic origin necessitates a reconsideration of the relationship of disease of the biliary tract to acute pancreatitis.

## THE PROBLEM OF ACUTE PANCREATITIS

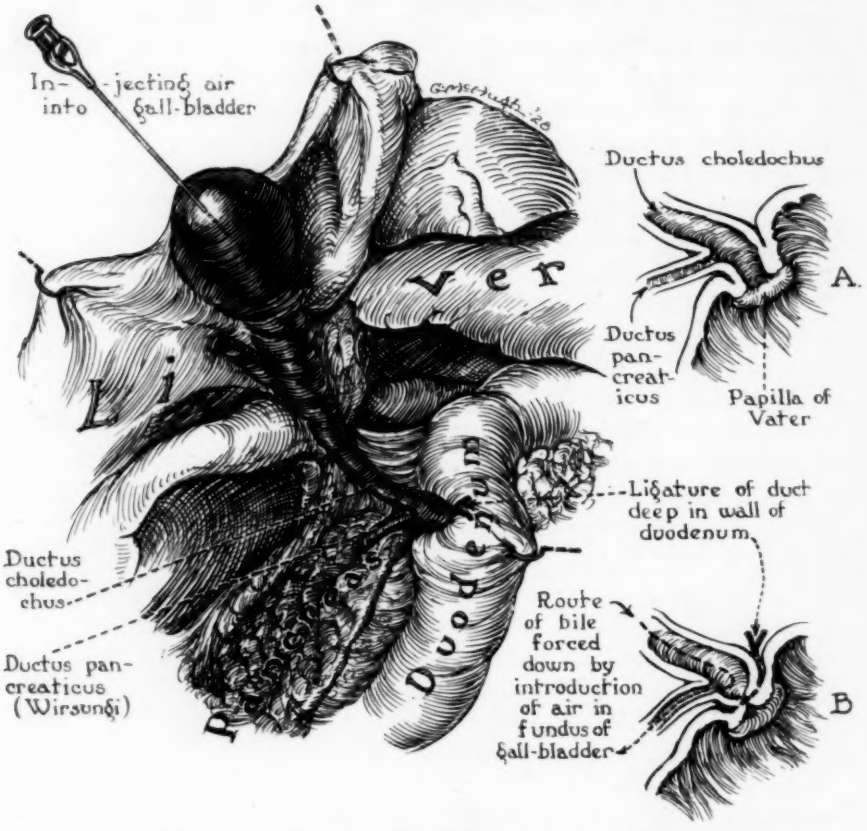
At necropsy Chirari not infrequently observed necrosis in the pancreas of patients in whom during life no symptoms of acute pancreatitis had been present, and he formulated the idea of self-digestion as the cause of pancreatitis. Postmortem necrosis of the pancreas is readily differentiated from actual pancreatic necrosis through the lack of cellular reaction in and surrounding the areas of necrosis. The proteolytic ferment of the pancreas, trypsinogen, is inactive in the pancreas and normally acquires the power to digest protein only when rendered active by succus entericus in the duodenum. Collection of the secretion from a pancreatic fistula has determined the accuracy of this observation for man as well as for the dog. A number of substances, however, exhibit the ability to convert trypsinogen into active trypsin. Experiment in vitro has determined that calcium salts (Delezenne), pressed liver juice and amino-acids (Wohlgemuth), as well as a number of other substances, possess this property. According to Delezenne, Fürth and Schütz, bile activates trypsinogen only when the pancreatic juice already exhibits a slight digestive action for protein, and Lattes found bacteria and leukocytes to have practically no activating influence for trypsinogen. Experiment in vivo, viz., injection into the pancreatic duct, has shown that of substances that concern the living organism, bile and duodenal content preeminently exhibit this property.

Following the injection of sterile bile or duodenal content into the pancreatic duct, acute pancreatitis almost regularly ensues. Polya found that the injection of 1 cc. of active trypsin into the pancreatic duct resulted in acute pancreatitis, whereas the injection of inactive substances such as inactivated trypsinogen, physiologic solution of sodium chloride or blood serum, even to the extent of rupture of the ducts, failed to produce the disease.

Rosenbach produced hemorrhages in the frog's tongue following the lingual injection of active trypsin, and Kirchheim and Matthes observed local hemorrhage and edema following the injection of trypsin into the vein of the ear of a rabbit, as well as hemorrhages and edema in the lungs. Trypsin, then, apparently possesses the property of digesting living tissue. Camus and Gley have been able to collect active trypsin from the pancreatic duct under the influence of stimulation of the vagus.

The presence of active trypsin in the pancreatic ducts alone, however, does not appear to be sufficient criterion for the production of the disease.

The study of the problem of acute pancreatitis, therefore, resolves itself into a consideration of how the pancreatic ferment may become activated within the gland so as to permit of self-digestion under condi-




A. Cross section: relation of duct of Wirsung to common duct and papilla of Vater
B. " " " " ducts with papilla of Vater tied off

Fig. 1.—Establishment of a common channel of the common bile and pancreatic ducts by placement of a ligature at the ampulla. Overdistention of the gallbladder with air causes contraction and emptying of the gallbladder with projection of bile into the pancreatic duct. An intravesical pressure in the gallbladder of 60 mm. of mercury is necessary to effect evacuation, but retrojection of bile into the pancreatic duct from the choledochus occurs at pressures physiologic for the biliary tract (from 210 to 240 mm. of pressure of bile in the common duct).

tions that come within the scope of functional or anatomic alterations in the human organism. In this report, we have been concerned primarily with an investigation of the rejected bile and lymphatic factors.

METHOD OF STUDY

These experiments, extending over five years, were done almost entirely on cats. Two hundred and eighty-nine animals were used; only ten dogs were used, and only in those experiments concerned with the effect of trauma in the genesis of pancreatitis. The cat is favorable for the investigation of the biliary reflux factor, in that the major pancreatic duct empties into the terminal end of the choledochus. By careful incision of the duodenal wall over the terminal end of the common bile duct, an extramucosal exposure of this point of union is easily made, and a ligature placed distally converts the two into a common channel. When this study was first commenced we were interested in determining whether normal bile projected into the pancreatic duct under the influence of the contraction of the gallbladder would give rise to an acute

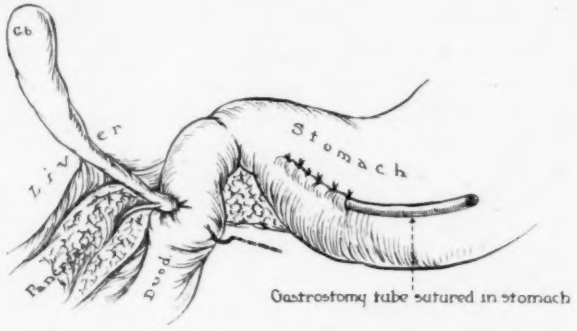



Fig. 2.—Establishment of a common channel of the common bile and pancreatic ducts with a gastrostomy tube in the stomach for feeding. A high incidence of pancreatitis was obtained by feedings of milk, cream and olive oil (fifteen of thirty-one, or 48.7 per cent). After excision of the gallbladder, this incidence was reduced (three out of eleven, 27.2 per cent) with feedings of fat, but was still higher than when dextrose, alcohol or protein were fed with the gallbladder in situ.

pancreatitis. The ejection of bile from the gallbladder was effected by overdistending this viscus by the introduction of air into the fundus with a fine hypodermic needle and a syringe. Following overdistention of the gallbladder, the latter contracted, and droplets of bile and air together passed over into the pancreatic duct, usually only into the beginning of the pancreatic duct, but occasionally well into the duct in the midportion or tail of the gland. In a few cats, methylene blue (methylthionin chloride, U. S. P.) was injected into the gallbladder instead of air, and the pressure at which the methylene blue-stained bile was regurgitated into the pancreatic duct was ascertained as well as the pressure necessary to effect an emptying of the gallbladder.

A number of experiments were also performed in which a common channel was established by placing a ligature at the ampulla, but without introducing anything into the biliary duct system. A gastrostomy of the Witzel type was done in these cats, and frequent feedings of milk, cream and olive oil and bile salts were given through the gastrostomy tube to effect a contraction of the gallbladder. The effect of feedings of dextrose, alcohol and a diet high in protein through a gastrostomy tube in cats with a common channel of biliary and pancreatic duct was studied. In another series of cats, fatty meals were administered through the tube after excision of the gallbladder.

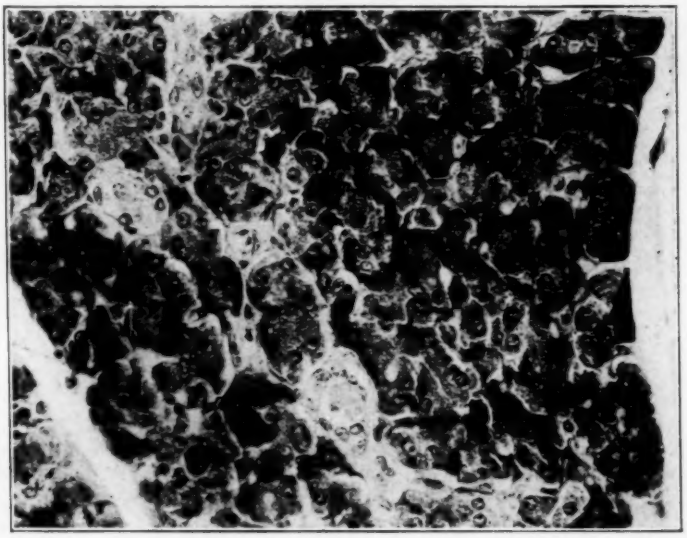


Fig. 3.—Normal pancreas of a cat; × 250.

In several cats, infection was established in the biliary passages by making an anastomosis between the stomach and the gallbladder. Cholecystitis and cholangeitis were almost constant accompaniments following cholecystogastrostomy. In some of these experiments, the major pancreatic duct also was tied. In a number of other cats, bacteria and gauze or unsterile human gallstones and gauze were placed in the gallbladder. Ligation of the major pancreatic duct was also performed in a few of these procedures. In these experiments, we were anxious to determine whether the establishment of acute infection in the biliary tract would result in acute pancreatitis. In a few instances, bacteria were injected directly into the substance of the pancreatic gland.

The influence of a combination of factors which were ineffective in producing pancreatic necrosis when operating as single factors was also ascertained, such as ligations of the pancreatic duct plus the subcutaneous

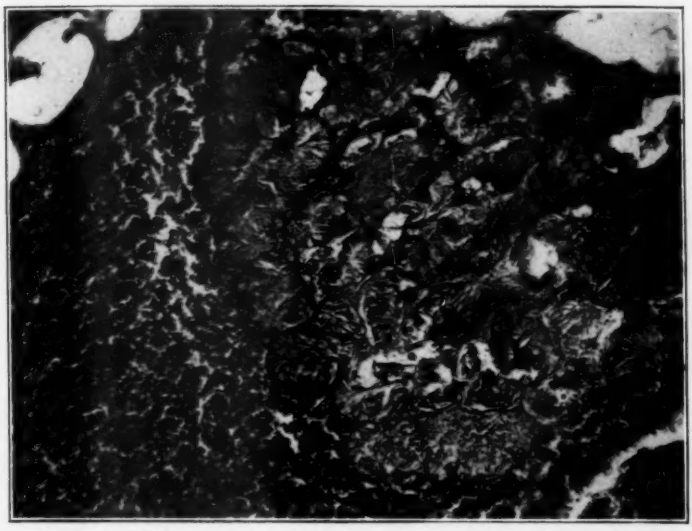


Fig. 4.—Fat necrosis of the omentum with leukocytic wall after the projection of bile into the pancreatic duct consequent on overdistention of the gallbladder in the presence of a common channel of the common bile and pancreatic duct; × 250.

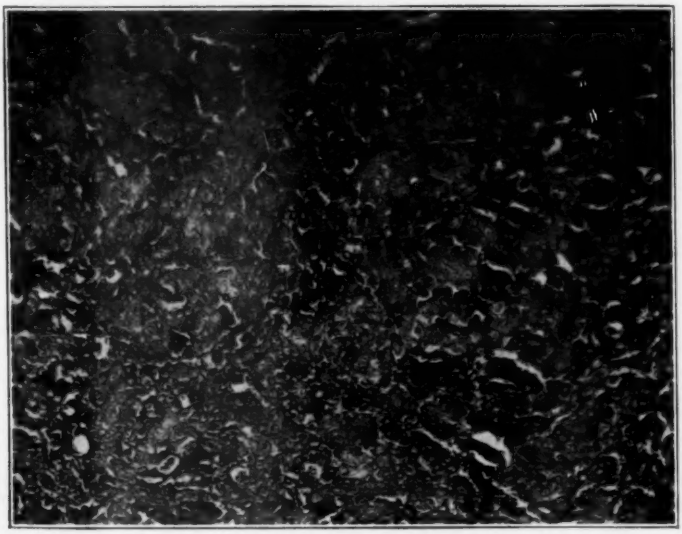


Fig. 5.—Pancreatic necrosis after the same procedure as in figure 4. The loss of contour of pancreatic acini with dissolution of the pancreatic substance is well shown; × 100.

administration of pilocarpine in physiologic doses; injections directly into the pancreatic substance plus ligations of the pancreatic duct or chemical stimulation of the vagus with pilocarpine.

In several cats and dogs, trauma to the pancreas was caused by complete division of the gland, division of the major ducts or crushing of the gland with a crushing clamp.

All experiments were done under ether anesthesia with aseptic technic. In the animals that died, necropsy was performed, usually directly following the death of the animals; a number were killed when it was apparent that death was imminent. In each experiment the pancreas was examined grossly and microscopically for evidence of pancreatic necrosis. Blocks of pancreatic tissue were embedded in paraffin and the sections were stained with hematoxylin and eosin.

## SUMMARY OF RESULTS

The outcome of the experiments appears in the accompanying tables, and will not be described in detail. All the gross criteria of pancreatic necrosis, viz., hemorrhage in the pancreas, subperitoneal fat necrosis and free fluid in the peritoneal cavity did not occur in many instances. In four of the thirteen instances in which a common channel of pancreatic and common bile ducts was established and retrojection of bile obtained into the pancreas under the influence of contraction of the gallbladder brought about by overdistending this viscus with air, gross hemorrhages were apparent in the pancreas.

In one animal, death occurred about twenty minutes after the animal had fully recovered from the anesthesia or about an hour after completion of the operation. In this instance, bile could be seen in the tail of the pancreas, and small hemorrhages were present throughout the gland. No fat necroses, however, were apparent,[3] but microscopic evidence of necrosis in the peripancreatic fat was present.

In two of these, the pancreas was fiery red throughout its greater portion. Hemorrhagic fluid in the peritoneal cavity was present in one of these cats. Gross hemorrhages were also seen in the instances in which active tryptic ferment was injected into the pancreatic duct as well as after the direct injection of bile into the pancreatic duct. In the majority of the experiments, therefore, the single gross evidence of pancreatic necrosis present was fat necrosis over the pancreas. In each instance, however, the pancreas was examined microscopically with extreme care, to make certain that microscopic evidence of actual

3. Following the production of acute pancreatic necrosis in dogs, Seidel found that fat necroses were present only when the period of survival was more than twelve hours.

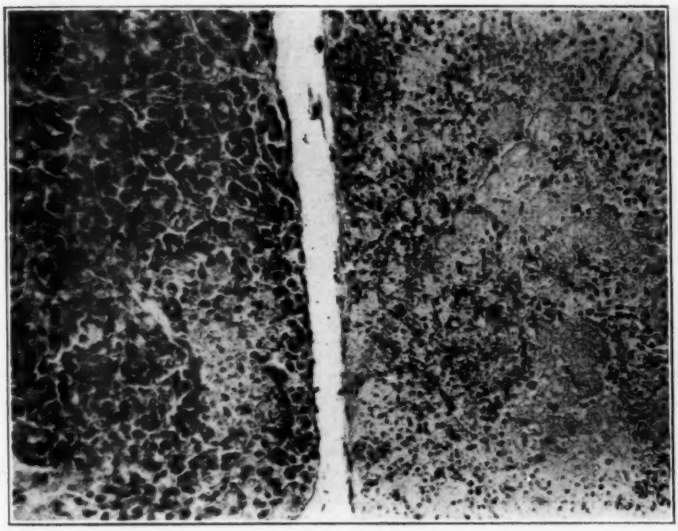


Fig. 6.—Pancreas of a cat following the injection of bile into the pancreatic duct. The pancreatic tissue on the left exhibits slight injury, whereas the cellular reaction and necrosis in the pancreas on the right side is far greater; × 100.

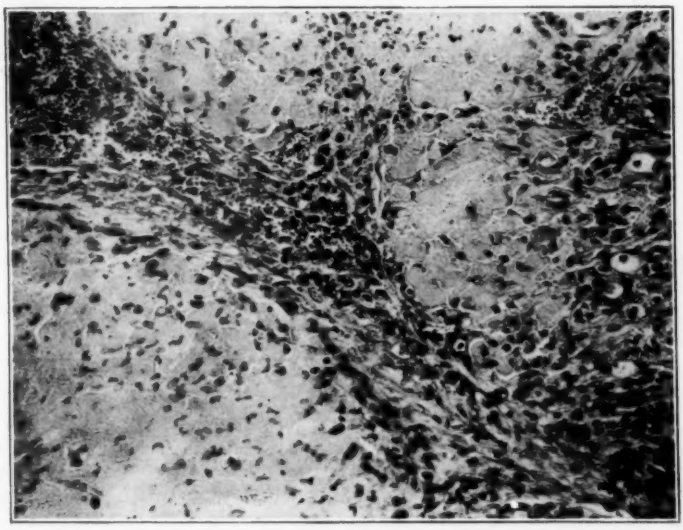


Fig. 7.—Pancreas of a cat following the injection of physiologic solution of sodium chloride into the pancreatic duct and the injection of bile into the pancreatic substance, showing necrosis, hemorrhage and leukocytic infiltration; × 100.

pancreatic necrosis was present. The necessity for differentiating postmortem autolysis from pancreatic necrosis has been referred to, and in each instance in which fat necroses over the pancreas were observed grossly and no microscopic cellular reaction was found in the pancreas

TABLE 1.—*Establishment of a Common Channel of Bile and Pancreatic Ducts by Ligature at Ampulla*

| Type of Operation | Number of Experiments | Positive Gross Changes | Positive Microscopic Changes |
|---|---|---|---|
| 1. Simple ligature at ampulla | 7 | 1 | 1 |
| 2. With injection of air | 13 | 8 | 8 |
| 3. With infection of gallbladder with agar streptococci and gauze | 4 | 3* | 1 |
| 4. Common channel plus gastrostomy and feedings of cream, olive oil and bile salts | 31 | 18 | 15 |
| 5. Same as 4 but feedings of dextrose | 9 | 2 | 2 |
| 6. Same as 4 but feedings of alcohol | 9 | 2 | 2 |
| 7. Same as 4 but feedings of protein | 13 | 0 | 0 |
| 8. Same as 4 but with excision of gallbladder | 11 | 3 | 3 |
| 9. Same as 4 plus infection of gallbladder | 19 | 5 | 5 |
| 10. Same as 4 plus daily subcutaneous injections of 1 mg. of pilocarpine hydrochloric acid | 6 | 6 | 3 |
| 11. Same as 4 plus injection of iodized oil into gallbladder | 6 | 3 | 1† |
| 12. Same as 4 plus injection of 2 cc. of pancreatic extract into gallbladder | 3 | 1 | 1 |

* Two were postmortem necroses.
† No roentgen evidence of reflux into pancreatic ducts.

TABLE 2.—*Injection into Pancreatic Duct Followed by Duct Ligation*

| Fluid Injected | Number of Experiments | Positive Gross Changes | Positive Microscopic Changes |
|---|---|---|---|
| 1. Bile | 5 | 5 | 5 |
| 2. Pancreatin | 3 | 3 | 3 |
| 3. Saline | 13 | 3 | 1 |

TABLE 3.—*Ligation of Major Pancreatic Duct*

| Type of Operation | Number of Experiments | Positive Gross Changes | Positive Microscopic Changes |
|---|---|---|---|
| 1. Ligation of major pancreatic duct | 6 | 0 | 0 |
| 2. Same as 1, plus daily subcutaneous injection of pilocarpine hydrochloric acid, 1 mg. | 6 | 3 | 3 |
| 3. Same as 1, plus infection of gallbladder | 13 | 3 | 2 |
| 4. Same as 1, plus infection of gallbladder plus gastrostomy and feeding of fat | 4 | 2 | 1 |

or in the gross areas of fat necroses themselves, the result has been counted as negative.

Injection of bile into the pancreatic duct terminated similarly in the five experiments in which this procedure was practiced (table 2). In one cat, the injection of physiologic solution of sodium chloride into the pancreatic duct, followed by its ligation, terminated in the death of the animal (table 3). Scattered fat necrosis and microscopic evidence

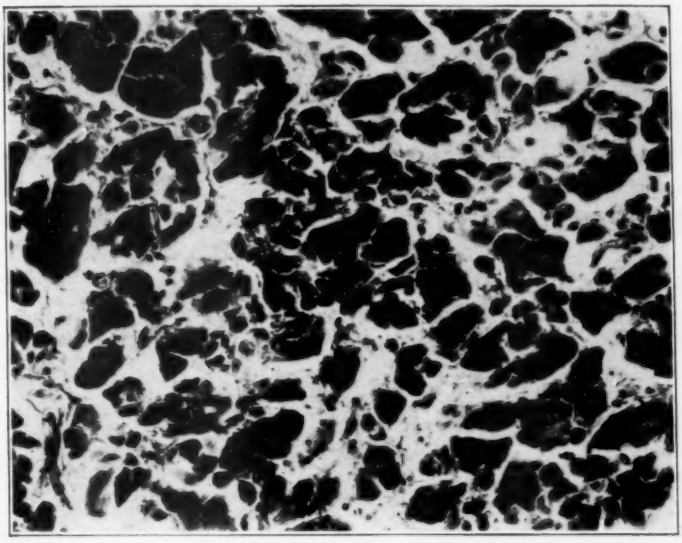


Fig. 8.—Interstitial edema of the pancreas after the injection of bacteria into the gland. A similar type of reaction may be seen following infection of the gall-bladder; × 250.

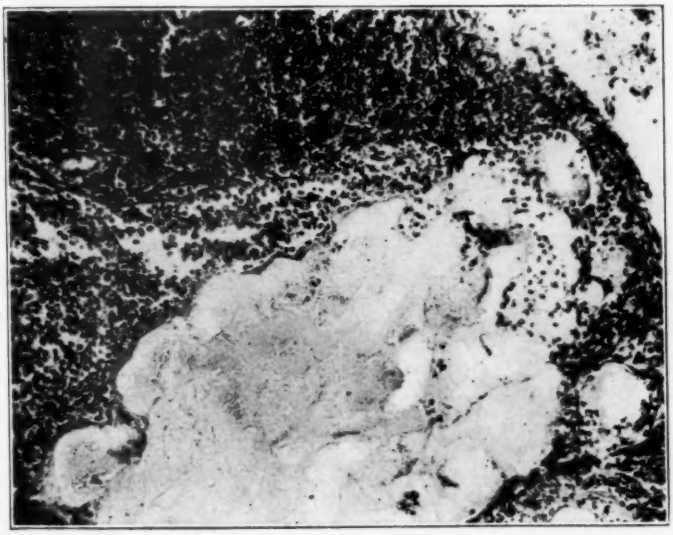


Fig. 9.—Necrosis in the pancreas of a cat and marked cellular reaction following ligation of the major pancreatic duct and daily subcutaneous administration of pilocarpine; × 100.

of damage to the pancreas were present in this instance. Attending the isolation of the duct, however, considerable trauma had occurred to the gland. Similar injections of the solution into other animals failed to produce acute pancreatitis.

Following cholecystogastrostomy, infection of the gallbladder regularly followed, and cholangeitis with abscesses of the liver was occasionally observed. The presence of intestinal worms in the gallbladder following such an anastomosis was not an infrequent observation. Although acute infection of the peritoneum occurred not infrequently, following the establishment of acute infection in the biliary passages by this method or after the introduction of septic foreign bodies into

TABLE 4.—*Infections of Gallbladder*

| Type of Operation | Number of Experiments | Positive Gross Changes | Positive Microscopic Changes |
|---|---|---|---|
| 1. Simple infection of gallbladder | 18 | 1* | 1* |
| 2. Same as 1, plus pilocarpine, 1 mg. subcutaneously | 8 | 0 | 0 |
| 3. Same as 1, plus gastrostomy and feeding of fat | 9 | 1 | 0 |
| 4. Same as 1, plus gastrostomy plus pilocarpine subcutaneously | 3 | 0 | 0 |
| 5. Same as 1, plus ligature at ampulla (see table 1, no. 3) | 4 | 3 | 1 |
| 6. Same as 1, plus ligature at ampulla, plus gastrostomy and feeding of fat (see table 1, no. 5) | 19 | 5 | 5 |
| 7. Same as 1, plus ligature of pancreatic duct (see table 3, nos. 3 and 4) | 13 | 3 | 2 |
| 8. Same as 7, plus gastrostomy and feeding of fat (see table 3, no. 4) | 4 | 2 | 1 |
| 9. Cholecystogastrostomy | 5 | 0 | 0 |
| 10. Same as 9, plus ligation of major pancreatic duct | 6 | 2 | 0 |

* In this animal bile was grossly evident in pancreatic ducts, a demonstration of the possibility of reflux in the absence of mechanical block at the ampulla.

the gallbladder, only once was positive evidence of pancreatitis obtained, and in this instance bile was seen in the pancreatic ducts despite the absence of organic obstruction at the ampulla. When the major pancreatic duct was ligated, in addition to the establisment of the biliary infection, definite evidence of pancreatic injury was obtained in a few instances (table 4). Not uncommon observations following the establishment of biliary infection were a loss of definite contour of the pancreatic acini, with an edema or swelling of the interstitium. Hemorrhage, pancreatic necrosis or fat necrosis with microscopic cellular reactions, however, were not seen.

In one instance, following the direct injection of bacteria into the gland, definite microscopic evidence of necrosis was present thirty days later. However, when the animal was killed it was found to be in

good health, and no gross evidence of acute pancreatitis was present at autopsy. In one dog in which biopsy was done on the pancreas a little more than two hours after the injection of bile into the substance of the gland, the pancreas appeared hemorrhagic, and definite microscopic evidence of necrosis of the gland was present. In another dog, though the animal survived and no marked gross alteration in the gland was seen, microscopic examination demonstrated acinar destruction.

Though death of the animal not infrequently followed pancreatic division or crushing, a definite acute pancreatitis occurred only once. The escape of pancreatic juice into the peritoneal cavity in the presence

Fig. 10.—Fibrosis of the pancreas after crushing with a Payr clamp; × 100.

of the trauma incident to operation did, as one should expect, frequently result in the death of the animal. In such instances, fat necroses were often present, but the pancreatic gland itself remained normal.

## COMMENT

In the procedures in which acute pancreatitis followed the injection of bile into the pancreatic duct, or its retrojection under the influence of contraction of the gallbladder, the time factor required for the production of the disease requires comment. It need scarcely be mentioned that the death of the animal following the establishment of a common channel of bile and pancreatic ducts does not signify a positive result. That small animals, such as the cat, survive occlusion of the common bile duct for only a short time is well known.

It was noted, however, that even though pancreatic necrosis occurred in all five instances in which bile was injected into the major pancreatic duct, followed by ligature of the duct, the period of survival was longer than in the animals in which the acute pancreatitis was produced by overdistention, and the subsequent contraction of the gallbladder, in the presence of a common channel. Undoubtedly, the absence of obstruction to the choledochus, when the injection is made directly into the pancreatic duct, permits of a longer survival.

The establishment of a common channel alone by ligation beyond the point of juncture of the two ducts was followed by a positive result

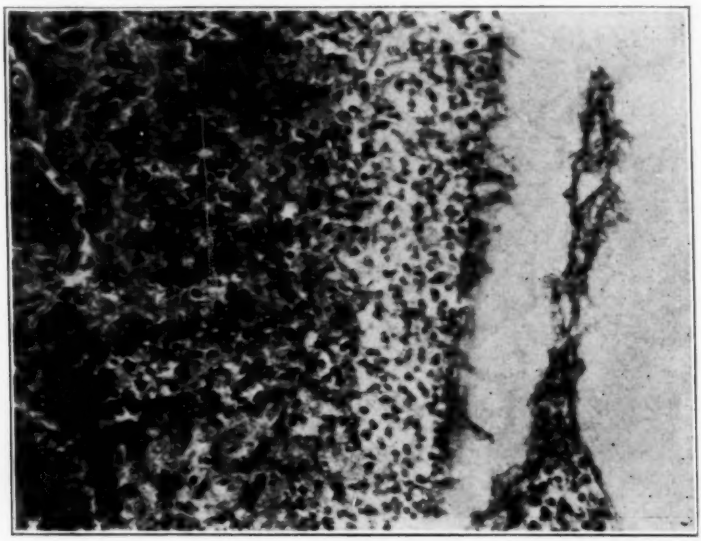


Fig. 11.—Necrosis of the pancreas with cellular reaction following the establishment of a common channel of the common bile and pancreatic ducts by placement of a ligature at the ampulla and feeding of fatty meals through a gastrostomy tube; × 100.

only once in the seven instances in which this procedure was done. In the thirteen experiments in which an emptying of the gallbladder was effected by the injection of air into the gallbladder, a positive result was noted eight times. In five other cats, the pressure at which the regurgitation occurred was ascertained by inserting a needle into the common bile duct just proximal to the ligature at the ampulla, but distal to the point of juncture of the pancreatic and bile ducts. A water manometer was employed to measure the pressure. Methylene blue instead of air was then introduced into the gallbladder with a 20 cc. Luer syringe through a needle puncture in the fundus of the gallbladder.

The tension in the gallbladder was measured with a mercury manometer. The pressure necessary to effect a contraction and emptying of the gallbladder was surprisingly great. The lowest intravesical pressure at which emptying of the gallbladder occurred under the influence of overdistention was 60 mm. of mercury; in one instance, a pressure of 80 mm. of mercury was necessary to effect contraction and emptying. However, regurgitation of bile from the common bile duct into the pancreatic duct occurred at much lower pressures. In one instance, slight regurgitation occurred at a pressure of 190 mm. of water. In the other experiments, regurgitation began at a pressure of from 210 to 240 mm. of water. Following contraction of the gallbladder, the pressures in the common bile duct rose suddenly to from 350 to 570 mm. of water and occasionally to as high as 800 mm. At pressures of from 350 to 570 mm. of water in the common bile duct, regurgitation into the pancreatic duct was regularly observed.

Later, however, we found that pancreatic necrosis could be produced with a fair degree of regularity by effecting a contraction of the gallbladder under the influence of a fatty meal of cream and olive oil fed through an opening produced by gastrostomy.[4] In the thirty-one instances in which this operation was done, positive evidence of pancreatic necrosis was obtained fifteen times. The rarity with which evidence of pancreatic necrosis was observed following simple establishment of a common channel of the bile and pancreatic ducts by placing a ligature at the ampulla (once in seven experiments) and its more frequent occurrence (fifteen times in thirty-one experiments) when fatty meals were added by feeding through a gastrostomy tube bespeaks the significance of the easier activation of the pancreatic ferment at the height of digestion. That the contraction of the gallbladder under the influence of the fatty meal may in part have been responsible for this increased frequency with which pancreatitis occurred following the establishment of a common channel of bile and pancreatic ducts, although no roentgen evidence of the regurgitation of bile from the gallbladder into the pancreatic ducts was obtained following preliminary injections of iodized oil into the gallbladder, is indicated by the lessened incidence of pancreatic necrosis after the excision of the gallbladder (three of eleven cats). Also, feedings of dextrose or alcohol failed to cause pancreatic necrosis with as great regularity as a fat diet. In thirteen cats in which a common channel was established, the feeding of protein failed to produce pancreatitis in a single instance. Hillyard[5] has indicated that feeding of the protein increases the secretion of bile more than any

4. Leven and Wangensteen: Proc. Soc. Exper. Biol. & Med. **27**:965, 1930.

5. Hillyard: Proc. Staff Meet. Mayo Clin. **5**:127, 1930.

other type of food. The series of cats fed fatty meals has been augmented to thirty-one animals, through the performance of experiments on three series which together equal in number those fed on a carbohydrate diet, in order to make certain that the incidence of pancreatitis after the feeding of fat occurred uniformly with such regularity.

The frequency with which this occurrence was observed after the feeding of fatty meals together with its lessened frequency after excision of the gallbladder serves to emphasize the significance of the contraction of the gallbladder for the development of pancreatitis in the presence of a common channel of pancreatic and common bile ducts. Though

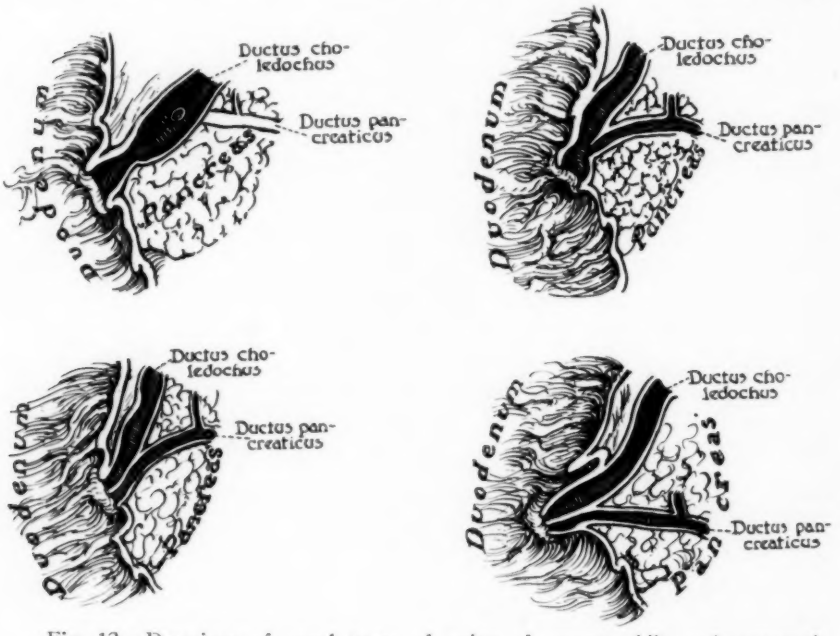



Fig. 12.—Drawings of usual types of union of common bile and pancreatic ducts in man (from Corning).

the factor of more effective activation by bile of the tryptic ferment of the pancreas in animals fed on a fat diet is not excluded, it appears unlikely that the latter possibility is of any moment, especially as when feedings of fatty meals through a gastrostomy tube were given to animals with infection of the gallbladder (table 4, no. 3) negative results were obtained in all of nine trials.

*Reflux of Bile.*—That the mechanism of the regurgitation of bile into the pancreatic duct, through the agency of a gallstone impacted in the ampulla, accounts for only a minority of cases of acute pancreatitis, needs no emphasis. In an inquiry made by Guleke in 1924, on 437 cases

of acute pancreatitis collected from 38 German surgical clinics, calculous obstruction at the ampulla was present in only 1.4 per cent of the total number. In Schmieden and Sebening's larger and more recent statistical study of 1,278 cases, 4.4 per cent exhibited a gallstone at the papilla. Stones were present in the common bile duct in 5 per cent of Guleke's cases, and in 13.6 per cent in Schmieden and Sebening's cases. Even when cognizance is taken of the fact that the obstructing calculus may have slipped back into the common duct or may have been extruded into the duodenum (Williams and Busch, Zoeppfel and others), it is apparent that the reflux of bile through such an agency accounts for only a small proportion of cases of acute pancreatitis.

In their study, Mann and Giordano found that the anatomic possibility for a reflux of bile into the pancreatic duct obtained in only 3.5 per cent of 200 cadavers. Most anatomic investigations have shown that a common ampullary termination of the choledochus and major pancreatic duct occurs in the majority of instances. Opie found such a communication in 89 of 100 cadavers; Baldwin observed a common ampulla in 70 of 90 dissections (78 per cent), and in 32 of 43 specimens examined by Ruge (75 per cent), a common termination of the two ducts existed.

Opie recognized that the possibility for a reflux of bile did not obtain in each instance in which an ampulla was present, but believed that such a regurgitation could occur in about one third of the cases. By injecting a dye opaque to the roentgen rays directly into the distal portion of the pancreatic duct, in the tail of the gland, Schmieden and Sebening found that a filling of the choledochus occurred in 8 of 35 instances (22.8 per cent).

We should like to refer to the experiments of Cameron and Noble,[6] reported from this laboratory with reference to the possibility of such a reflux. They introduced a small biliary calculus, 3 mm. in diameter, into the hepatic duct of 100 fresh necropsy specimens, and pushed the calculus into the terminal portion of the choledochus. The hepatic duct was then connected with a reservoir of water and a manometer, and water was forced into the hepatic duct at a pressure of about 100 mm. of water. In 66 instances, a reflux of bile occurred into the pancreatic duct. In 74 of the 100 instances, an ampullary communication was present; in 8 of these, the duodenal orifice was so large that the calculus was extruded into the duodenum. It is evident, therefore, that the anatomic possibility for this reflux obtains with far greater frequency than the measurements made by Mann and Giordano on specimens fixed in formaldehyde would indicate.

6. Cameron, A. L., and Noble, J. F.: Reflex of Bile up the Duct of Wirsung Caused by an Impacted Biliary Calculus, J. A. M. A. **82**:1410 (May 3) 1924.

Archibald has adequately demonstrated for the cat that the sphincter of Oddi can withstand pressures that would permit the regurgitation of bile into the pancreatic duct, in the absence of organic obstruction at the ampulla. Mann and Giordano, however, were unable to produce pancreatitis when bile was run into the pancreatic duct under gravity pressure, at pressures physiologic for the biliary tract.

Mann and Giordano found that the intraductal pressure in the choledochus of the dog rarely exceeded a pressure of 350 mm. of bile. Bile is secreted continuously, whereas pancreatic juice is secreted intermittently, but at pressures similar to those in the biliary tract, according to Mann and Giordano. In unanesthetized dogs during digestion, Harms, of Guleke's clinic in Jena, has recently reported higher pressures in the pancreatic duct than in the common bile duct. This observation, Guleke believes, is further evidence against the reflux of bile as a frequent etiologic factor of acute pancreatitis. Although the onset of acute pancreatitis not infrequently follows fairly directly the ingestion of an unusually large meal, bile cannot be regurgitated into the pancreatic duct under normal circumstances; if that were possible, many of us would live in constant dread of this potential danger. Mann and Giordano have shown, however, that during retching or vomiting, the pressure in the choledochus may attain 1,000 mm. of bile.

Westphal was able to demonstrate in several laboratory animals that electrical stimulation of the vagus or of the sympathetic causes disturbances in the tone of the gallbladder and its ducts, as well as in the sphincter of Oddi. Such changes were also elicited following the administration of drugs that influence the sympathetic or parasympathetic nerves. Disturbances in the contractile tone of the biliary ducts and ampullary sphincter mechanism have been called into question by Westphal as the stasis factor contributing to the formation of gallstones. This opinion is shared by Aschoff and has also received the approbation of others. Rost expressed the belief that in many instances of icterus without demonstrable mechanical obstruction a disturbance in the sphincteric arrangement at the terminal end of the common bile duct may be responsible.

Giordano and Mann [7] recently found a thickening of the terminal end of the common bile duct, with an increase in muscle tissue in some instances of duodenal ulcer and cholecystitis. They suggested that this thickening may cause loss of function or spasm. In the latter event, however, they are of the belief that both the pancreatic and common bile ducts would be occluded.

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7. Giordano, A. S., and Mann, F. C.: Sphincter of Choledochus, Arch. Path. **4**:493 (Dec.) 1927.

That an imbalance in the musculonervous control at the ampulla might operate to effect a regurgitation of bile into the pancreatic duct is easily understandable. That regurgitation of bile actually occurs through such an agency, however, remains to be demonstrated.

Archibald's production of a regurgitation of bile in the cat concerns acute experiments under artificial circumstances. We have been unsuccessful in many attempts to effect such a regurgitation in the cat in the absence of a mechanical block at the ampulla. In one instance, however, following the establishment of infection in the gallbladder, regurgitation occurred without the existence of an obstruction at the ampulla (table 4, footnote).

The more frequent regularity with which pancreatic necrosis may be produced by injections of bile, duodenal content or other substances into the pancreatic duct, at the height of digestion, has been noted by many investigators. It has already been pointed out that acute pancreatitis is found to have its onset directly following a large meal, and often a fatty meal, and the increased frequency with which pancreatitis was produced in the presence of a common channel of pancreatic and common bile ducts when fat was fed and the decreased incidence after excision of the gallbladder lend credible support to the contraction of the gallbladder as being the significant factor rather than the performance of the experiments at the height of digestion. It is well known that patients with disease of the gallbladder are usually intolerant of fatty foods.

It has already been indicated that trypsin has the power to digest living tissue. In connection with the consideration of the biliary factor, it should also be recalled that Tatum [8] was able to demonstrate a marked cytolytic activity for bile on tissue by immersing small blocks of various tissues in bile at body temperatures. Sellards [9] observed local necrosis following the injection of bile into the salivary glands, and Binet has made the same observation for bile introduced subcutaneously. Following the direct injection of bile into the pancreas, we noted microscopic necrosis and hemorrhage in the gland. This activity of bile, combined with the injury to the smaller ducts in the pancreas attending ampullary occlusion, is undoubtedly a factor that aids the dissemination of the activated pancreatic ferment throughout the gland, resulting in its digestion when bile is retrojected into the pancreatic duct.

In connection with the factor of the reflux of bile as a causative agent of acute pancreatitis, the possibility of an ascending infection from the duodenum should be mentioned. It has been adequately demonstrated that the injection of duodenal content into the pancreatic

8. Tatum: J. Biol. Chem. **27**:243, 1916.
9. Sellards: Bull. Johns Hopkins Hosp. **19**:268, 1908.

duct may cause acute pancreatitis. Although Seidel has shown that the establishment of duodenal obstruction in the dog may permit the regurgitation of duodenal content into one of the pancreatic ducts, the origin of acute pancreatitis in man, through such an agency, is undoubtedly an uncommon event, even though the duct of Santorini opens into the duodenum without a sphincteric closure mechanism. Williams and Busch found that the discharge of a gallstone through the ampulla of Vater left the latter patulous, so that the possibility for regurgitation of duodenal content into the pancreatic duct was present. The occasional occurrence of acute pancreatitis in the presence of a duodenal diverticulum in juxtaposition to the terminal end of the common bile duct may have its explanation in such an origin. The migration of an intestinal parasite, especially the ascaris, through the duodenal ampulla into the pancreatic duct, is not so unusual. Schmieden and Sebening stated that about fifty such instances are to be found reported in the literature.

*Lymphatic Factor.*—As concerns the lymphatic factor, it is important that pancreatic necrosis did not once follow the establishment of acute infection in the biliary tract. Neither did we cause pancreatic necrosis by the direct injection of bacteria into the pancreas. Polya made injections of bacteria into the pancreatic duct in twelve dogs, and only once succeeded in producing an acute hemorrhagic pancreatitis. Interstitial inflammation or abscesses not infrequently resulted.

The frequency with which acute pancreatitis follows on a so-called "acute gallbladder attack" is well known. Many patients suffering from acute pancreatitis state that in its onset such an attack has been indistinguishable from previous similar attacks of disease of the gallbladder. However, when such patients come to operation, an acute inflammation in the gallbladder is usually not found, even though it may obviously be diseased and contain stones. In hyperacute cholecystitis, such as occurs in phlegmonous or gangrenous inflammations, the complication of clinical acute hemorrhagic pancreatitis is also unusual. It is in this latter type of inflammation in the biliary apparatus that one should expect to find the association of acute pancreatitis, if spread of the infection by the lymphatics played a prominent rôle in the etiology of acute pancreatitis. Lymphangitis in acute infections, especially those of a streptococcic nature, is a common occurrence, and spread of infection by this route is generally feared. The absence of this danger in chronic infections is also generally conceded.

Whereas Franke, Barthels and other earlier investigators have declared the existence of direct lymphatic communication between the biliary apparatus and the pancreas, Kodama failed to observe them.

Kaufmann has commented on the experimental proof that the investigations of Graham and Peterman have lent to the lymphatic theory. Kaufmann found that in those instances in which bacteria were present in the pancreas following intraportal injections of bacteria or the establishment of acute infection in the gallbladder a bacteremia was also usually present. The more important consideration, however, is that isolation of bacteria from the pancreas is not synonymous with pancreatic necrosis. The crucial test is whether or not an actual pancreatic necrosis follows. It has already been indicated that though cloudy swelling was a regular observation in the gland following the establishment of acute infection in the gallbladder, pancreatic necrosis did not once follow.

In 1911, Arnsberger stated that since surgical intervention had been practiced more frequently for acute cholecystitis, edema and infiltration of the mesenteries in the upper part of the abdomen, as well as swelling and edema of the pancreas, were not infrequently to be seen. He was not certain, however, that this alteration in the pancreas concerned an actual pancreatitis, and referred to the fact that Kehr had previously designated the condition merely as pancreatic swelling. Arnsberger believed that it concerned infection going out to the pancreas from the biliary passages by way of the lymphatics, and described the condition as "lymphadenitis pancreatica."

More recently, Arnsberger reported four such cases, and described the presence of fat necrosis without demonstrable pancreatic necrosis. Zoeppfel also observed instances of the same character, but expressed the belief that this glassy edema and swelling of the gland, associated with fat necrosis, were the precursors of acute hemorrhagic pancreatitis. In two of four such cases seen by Zoeppfel during "acute gallbladder attacks," biopsy showed no evidence of injury to the pancreatic cells.

What Arnsberger and Zoeppfel observed and described would appear to correspond with what obtains in the experimental animal following the establishment of acute infection in the biliary tract.[10] Swelling and edema may obtain, but the well known picture of acute pancreatic necrosis does not occur.

Zoeppfel's belief that the edema and swelling of the pancreas observed occasionally in so-called "acute gallbladder attacks" are precursors of actual hemorrhagic pancreatitis is an important consideration in the interpretation of the pathogenesis of acute pancreatitis, and cannot be

10. In a recent article entitled "Acute Edema of the Pancreas (Ann. Surg. **90**:803, 1929), Archibald also called attention to these pancreatic changes, but stresses their occurrence as an accompaniment of regurgitations of bile that do not go on to pancreatic necrosis. DeWitt Stettin (Ann. Surg. **92**:284, 1930) supports the contention of Zoeppfel that acute edema of the pancreas is a forerunner of the more dangerous acute hemorrhagic pancreatic necrosis.

passed over lightly. If Zoeppfel's contention is correct, the frequent association and relation of disease of the gallbladder to acute pancreatitis are at once understandable.

As has been indicated, microscopic swelling and edema of the pancreas are not uncommon accompaniments of acute inflammations of the gallbladder in the experimental animal. It is clear, however, that these experimental pancreatic changes do not eventuate in acute pancreatic necrosis. A sufficient number of observations regarding the frequency of these changes of swelling and edema following acute cholecystitis have not accumulated to indicate the regularity of their occurrence as accompaniments or complications of acute biliary infection. In 115 cases of acute cholecystitis submitted to immediate operation during the acute stage by Zoeppfel, 11 showed evidence of pancreatic injury. At least this much is true: With the widely practiced conservative treatment for acute cholecystitis, even should these pancreatic changes obtain frequently, their termination in actual pancreatic necrosis must be an unusual occurrence; otherwise, death from acute pancreatitis as a complication during the course of acute cholecystitis should be a frequent observation. On the contrary, the relative safety of using conservative treatment in most cases of acute cholecystitis is well known.

The facts that the mortality in the type of case referred to by Arnsberger and Zoeppfel is very low (no mortality in the eight cases reported by them in which operation was performed), and that even in cases of acute hemorrhagic pancreatitis in which operation is performed the day of inception of the symptoms this figure approaches 50 per cent, would indicate that the two are fairly distinct entities.

The belief that acute pancreatitis is not the result of infection, and that necrosis is the primary phenomenon, that hemorrhage and inflammation are secondary to necrosis, occasioned Opie and Meakins to substitute the name pancreatic necrosis. This designation has been in general use in German medical literature for many years. The term "acute pancreatitis" is employed in German medical literature for only that group of pancreatic diseases which are thought to have an underlying inflammatory etiology.

To be certain, no strict pathologic distinction can be drawn between these forms of the disease. Hemorrhage in the gland in pancreatic necrosis is not a necessary accompaniment or a criterion of the grade of necrosis of the gland. In most cases of actual pancreatic necrosis, hemorrhages are present, but fatal instances in which no gross bleeding was present are well known. At the other extreme are those instances of pancreatic necrosis, commonly called pancreatic apoplexy, in which hemorrhage dominates the picture. The finding of bacteria in the pancreas in cases of actual hemorrhagic pancreatitis has been given as

evidence of the bacterial origin of the disease (Zoeppfel, Brütt). In early instances, however, bacteria are usually not found, and Tower [11] found bacteria regularly in the peritoneal cavities of dogs following the fatal issue attending the pancreatic necrosis consequent on the extensive ligature of pancreatic vessels. Tower's observations would indicate that infection was a terminal event. Guleke, who speaks from a considerable experimental as well as a broad clinical experience, is also in accord with this opinion.

Acute pancreatitis of distinct inflammatory origin cannot be discussed at any length here, but it should be mentioned that acute purulent pancreatitis or abscess occasionally has its origin in infections in the biliary tract, spreading to the pancreas by way of the pancreatic duct, by extension through contiguity or by way of the lymphatics. Metastatic abscesses during the course of acute infections such as diphtheria and scarlet fever, and especially mumps, are not unknown. Following the perforation of chronic peptic ulcer of the stomach, abscesses in the gland occasionally occur. The prognosis of suppurative lesions in the pancreas, though serious, is, as many statistical studies have shown, better than in pancreatic necrosis.

*Combination Factors.*—When the pancreatic ducts alone are obstructed, as Eppinger has shown, an accumulation of detritus occurs in the major ducts, resulting from the injury to the epithelium of the duct. Rupture of the acinar walls and hemorrhage in the interstitium may also occur. This damming back of secretion in the gland may be an important contributing factor in the genesis of acute pancreatitis. The occlusion of one duct would naturally not effect the changes in the gland observed following obstruction to both ducts, but in the human pancreas, as Opie has shown, the lesser duct of Santorini is often functionless or practically so. Nordmann was able to produce acute pancreatitis in the dog only through the agency of infection, when the entire outflow of secretion from the gland was blocked.

Injury to the pancreas undoubtedly occurs through obstruction of the pancreatic duct, and under the influence of an activating agent for trypsinogen pancreatic necrosis may obtain. Hess claimed to have produced acute pancreatitis, following occlusion of the pancreatic ducts, when the ligation was done at the height of digestion. Nearly all other investigators are in accord, however, that ligation of the pancreatic ducts usually results in atrophy and a sclerosing process in the pancreas. Previous to the assertion of Camus and Gley that stimulation of the vagus results in the secretion of active trypsin from the pancreatic cells, Opie had already produced pancreatic necrosis in two cats following

11. Tower, L. E.: Pathologic Physiology of Experimental Gangrenous Pancreatitis, J. A. M. A. **86**:1112 (April 10) 1926.

the ligation of both pancreatic ducts under the influence of chemical stimulation of the vagus with pilocarpine. More recently, Brocq and Binet were successful in three of four attempts to produce acute pancreatitis in dogs by this method.

Lattes has made the suggestion that the activation of trypsinogen is brought about by pancreatic necrosis, through whatever agent may cause necrosis of the gland. It was previously stated that Wohlgemuth found amino-acids capable of activating trypsinogen in vitro, and Lattes found pancreatic tissue itself quite potent in this respect. Whereas, theoretically, damaged pancreatic tissue may activate the tryptic ferment of the gland, experiment on the living animal demonstrates that this activation is usually insufficient to produce acute pancreatitis. Although pancreatic damage as the result of trauma, ligation of the duct or chemical or bacterial injury may rarely cause pancreatic necrosis when

TABLE 5.—*Injections into Pancreatic Gland Substances*

| Material Injected | Number of Experiments | Positive Gross Changes | Positive Microscopic Changes |
|---|---|---|---|
| 1. Bile | 11 (3 dogs) | 1* (dog) | 1* |
| 2. Saline | 5 | 2† | 0 |
| 3. Broth culture of killed typhoid bacilli | 3 (2 dogs) | 0 | 1 (dog) |
| 4. Bile into pancreatic substance and saline into pancreatic duct | 6 | 6 | 6 |
| 5. Bile into pancreatic substance plus daily subcutaneous injection of 1 mg. pilocarpine | 3 | 3 | 3 |
| 6. Bile into pancreatic substance plus ligation of major pancreatic duct | 4 | 2 | 2 |

* In the instance in which evidence of pancreatic necrosis occurred the animal was killed two hours, twenty minutes after the injection. All other animals survived the injection.
† Probably postmortem necrosis.

operating as single factors, it would appear that a combination of such factors may produce the disease.

When bile or bacteria were injected directly into the substance of the pancreas, microscopic evidence of pancreatic damage was obtained. All the animals survived the procedure, however, and the interstitial edema and swelling noted after the injection of bacteria into the gland and the occurrence of pancreatic necrosis and hemorrhage following the injection of bile were noted only after excision of a portion of the gland for biopsy from an animal that presented no unusual symptoms. When, however, bile was injected into the substance of the pancreas and saline through the pancreatic duct, a lethal outcome occurred in every instance (table 5, no. 4), with definite signs of pancreatic necrosis in each case. Similarly, when 1 mg. of pilocarpine was administered subcutaneously to animals into whose pancreas bile had been injected, a lethal pancreatic necrosis occurred in each instance (table 5, no. 5). When bile was injected into the pancreatic substance and the major

pancreatic duct also was occluded, two of four such animals died with pancreatic necrosis. Following trauma to the gland, necrosis of the pancreas is an uncommon occurrence. In man, rupture of the pancreas in acute pancreatic necrosis has resulted in only a few instances.

Whereas simple ligation of the major pancreatic duct alone failed to cause pancreatitis, in the six cats in which the major pancreatic duct was ligated and in which, in addition, pilocarpine was given subcutaneously, pancreatic necrosis was observed three times. The establishment of acute infection in the gallbladder and pilocarpine administered subcutaneously failed to produce the disease in eight trials. Feeding of fat through a gastrostomy tube in cats with acute infections of the gallbladder failed to bring about pancreatic necrosis in the nine cats in which this combination was tried (table 4, no. 3). Whereas in vitro infected bile activates

TABLE 6.—*Controls to Eliminate Trauma as a Factor*

| | Number of Experiments | Positive Gross Changes | Positive Microscopic Changes |
|---|---|---|---|
| A. Operative Procedures | | | |
| 1. Isolation of points of union of pancreatic and common bile ducts at ampulla without ligation with feeding through gastrostomy tube | 3 | 0 | 0 |
| 2. Ligation of common bile duct proximal to junction with pancreatic duct plus gastrostomy.. | 9 | 0 | 0 |
| 3. Gastrostomy and feeding alone..... | 3 | 0 | 0 |
| B. Direct Trauma to Pancreas | | | |
| 1. Crushing with Payr stomach clamp..... | 3 (2 dogs) | 1 (cat) | 1 |
| 2. Transverse division of gland..... | 8 (2 dogs) | 1 | 0 |
| 3. Division of major pancreatic duct..... | 4 (1 dog) | 0 | 0 |

trypsinogen with greater facility than sterile bile, we failed to secure evidence that indicated that this obtained in the living animal. Sterile bile regurgitated into the pancreatic duct in the presence of a ligature at the ampulla produced pancreatic necrosis eight times out of thirteen trials in the injection experiments (table 1), and fifteen times out of thirty-one instances when feedings were added to the establishment of a common channel. In only five out of nineteen trials did pancreatic necrosis occur under the same conditions when the bile in the gallbladder was infected. Of the factors which are impotent when operating as single agents but capable of producing the disease when acting jointly with another factor, obstruction of the pancreatic ducts, chemical stimulation of the vagus with pilocarpine and the presence of bile in the substance of the pancreatic gland appear to be the most important. The regularity with which pancreatic necrosis follows the injection of bile or pancreatin into the pancreatic duct (table 2, nos. 1 and 2) again bespeaks the importance of the effective activation of trypsinogen in the production of pancreatic necrosis.

Experimental investigations concerning the vascular factor in the production of the disease have shown that acute pancreatitis rarely follows unless the gland is extensively devascularized. Ligations of vessels, accompanied by plugging of some of the pancreatic vessels with air, lycopodium powder, oil, wax or other substances results in acute pancreatic necrosis, a method, however, which has no parallel in the living organism. Beneke postulated that pancreatic necrosis may be brought about by a temporary arrest of blood supply, such as may obtain through the agency of vessel spasm. He referred to experiments performed by Blume and himself, in which pancreatic necrosis was caused by squeezing the pancreas between the hands for twenty minutes. Undoubtedly, however, trauma is also an important contributing factor in such an experiment, without which pancreatitis could not have been produced.

## SUMMARY

The retrojection of bile into the pancreatic duct under the influence of contraction of the gallbladder produces pancreatic necrosis in the cat, with a fair degree of regularity. We have been able to effect this regurgitation in the cat by establishing a common channel at the ampulla accompanied by the feeding of fatty foods through a gastrostomy tube without the introduction of any substance into the duct system. In the absence of an obstruction at the ampulla, however, we have been unable to produce regurgitation of bile into the pancreatic duct. In man, reflux of bile into the pancreatic duct through the agency of a gallstone impacted at the ampulla has frequently given rise to acute pancreatitis, but this mechanism accounts for only a minority of instances of the disease. The anatomic possibility for such a reflux, however, obtains in a large percentage of persons, and it is possible that such a reflux may be conditioned through a disturbance in the sphincter-regulating mechanism at the ampulla. The actual occurrence of pancreatic necrosis through such an agency in man, however, remains to be demonstrated.

Following the establishment of acute infection in the biliary tract, cloudy swelling of the pancreas is regularly observed; an actual acute pancreatic necrosis, however, does not result. Clinically, pancreatic injury of a similar character appears to be an occasional accompaniment of acute infections of the gallbladder. That these pancreatic changes are precursors of pancreatic necrosis and eventuate in actual pancreatic necrosis proof is lacking; that in the presence of an activating influence for trypsinogen these pancreatic changes may eventuate in actual pancreatic necrosis appears to be substantiated.

The effective activation of trypsinogen would appear to be the essential factor in the production of the disease. Though pancreatic tissue and products of its disintegration may activate trypsinogen in vitro,

experiment on the living animal demonstrates that injury to the gland effected through ligation of the duct, infection or mechanical trauma is usually inadequate as a single factor to produce acute pancreatic necrosis.

The results of this study indicate the direction of subsequent investigations, viz., that the solution of the cause of probably a considerable number of instances of acute pancreatic necrosis is to be found in a combination of factors which when operating alone are inadequate to produce the disease.

## BIBLIOGRAPHY

A complete bibliography of the very extensive literature of acute pancreatitis is to be found in the following references:

Brocq, P.: Les pancréatites aigües chirurgicales, Paris, Masson et Cie, 1926.

Gross, O., and Guleke, N.: Die Erkrankungen des Pankreas. Enzyklopädie der klinischen Medizin, Berlin, Julius Springer, 1924.

Guleke, N.: Die neueren Ergebnisse in der Lehre der akuten und chronischen Erkrankungen des Pankreas mit besonderer Berücksichtigung der entzündlichen Veränderungen, Ergebn. d. Chir. u. Orthop. **4**:408, 1912.

Körte, W.: Die chirurgischen Krankheiten und die Verletzungen des Pankreas, Deutsche Chirurgie, Stuttgart, Ferdinand Enke, 1898, no. 45, p. 175.

Schmieden, V., and Sebening, W.: Chirurgie des Pankreas, Arch. f. klin. Chir. **148**:319, 1927.

Discussion of the paper of Schmieden and Sebening at the Fifty-First German Surgical Congress, Arch. f. klin. Chir. **148**:67, 1927.

# ASCENDING URINARY INFECTION

## AN EXPERIMENTAL STUDY *

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The routes by which infection may travel in reaching the ureter and kidney from the bladder are: (1) regurgitation of the contents of the bladder through the ureterovesical orifice, (2) direct extension through the wall of the ureter, (3) extension of the infection by way of the lymphatics and (4) by way of the blood stream.

From the clinical standpoint, Rovsing,[1] Israel,[2] Stoeckel,[3] Albarran,[4] Warschauer [5] and others believed that a stagnating urinary column due to ureteral obstruction favored the upward spread of organisms.

Rovsing [1] and Melchior [6] concluded: (1) that experimental cystitis could not be produced in animals without retention of urine or trauma to the bladder; (2) that with retention of urine experimentally produced, pyelitis as a rule did not result, and (3) that trauma to the bladder with or without retention of urine produced pyelonephritis.

Zeit [7] and Peterson,[8] in 1899, transplanted the ureters into the intestinal tract in 141 dogs and found that infection of the kidney eventually took place.

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* From the Department of Preventive Medicine, A. O. Smith Corporation.

1. Rovsing, T.: Ueber Aetiologie, Pathogenese und Behandlung der septischen Infection der Harnwege, Monatschr. d. Harnkr. u. sex. appar. **3**:505, 1898; Klinische und experimentelle Untersuchungen über die infectiöser Erkrankungen der Harnorgan, Berlin, Oscar Coblenz, 1898.

2. Israel, J.: Chirurgische Klinik der Nierenkrankheiten, Berlin, August Hirschwald, 1901.

3. Stoeckel: Verhandl. d. deutsch. Gesellsch. f. Urol. **2**:39, 1909.

4. Albarran, J.: Étude sur le rein des urinaires, Thèse de Paris, 1889.

5. Warschauer: Berl. klin. Wchnschr. **38**:398, 1901.

6. Melchior: Bericht über 52 bacteriologisch untersuchte Fälle von infectiöser Erkrankung des Harntractus, Monatsbl. d. Krankh. d. Harn- u. Sex. Appar. **3**:584, 1898.

7. Zeit: Pathology and Bacteriology of Uretero-Intestinal Anastomosis, Tr. Chicago Path. Soc. **4**:210, 1899-1901.

8. Peterson, R.: Anastomosis of Ureters with Intestine, Tr. Am. Gynec. Soc., 1900, p. 136.

Guyon and Albarran,[9] in 1890, injected charcoal into the bladder of dogs and ligated the urethra. They found charcoal in the pelvis of the kidneys in forty-eight hours, and pyelonephritis in some of these animals.

Lewin[10] and Lewin and Goldschmidt,[11] in 1893, injected milk, air or colored fluids into the bladder of rabbits with moderate intravesical pressure, and observed regurgitation of the contents of the bladder into the pelvis of the kidney.

Courtade and Albarran,[12] in 1894, using dogs, repeated Lewin and Goldschmidt's work and found that regurgitation of the bladder contents occurred; but they differed in their view as to what grade of intravesical pressure was most favorable to regurgitation. Sampson,[13] in 1906, working with dogs, was unable to confirm Lewin's observations and concluded: "The reflex of urine from the bladder into the ureter may be considered an etiological factor in the causation and maintenance of renal infection only when the intravesical portion of the ureter is diseased, thus impairing its function, or when some ureteral obstruction exists."

Hagner,[14] in 1912, first observed regurgitation of fluid from the bladder to the kidney during ureteral catheterization.

Kretschmer,[15] in 1915, observed clinically regurgitation of the contents of the bladder into the ureter in cystography. Direct extension of infection from the bladder through the wall of the ureter has been shown experimentally by Bauereisen.

### LYMPHOGENIC INFECTIONS

Mascagni,[16] in 1787, first described a lymphatic connection between the ureter and the kidney. Teichman,[17] in 1861, Sappey,[18] in 1874,

9. Guyon and Albarran, J.: Arch. de méd. exper. **2**:181, 1890.

10. Lewin: Die Uebertritt von festen Körpern aus der Blase in die Niere, Arch. f. exper. Path. u. Pharmakol. **40**:287, 1897.

11. Lewin and Goldschmidt: Versuche über die Beziehungen zwischen Blase, Harnleiter und Nierenbecken, Virchows Arch. f. path. Anat. **134**:33, 1893.

12. Courtade and Albarran: Sur le réflex du content vesicle dans les uréters, Ann. d. mal. d. org. génito-urin. **12**:561, 1894.

13. Sampson, J. A.: Ascending Renal Infection, Bull. Johns Hopkins Hosp. **14**:334, 1903.

14. Hagner, F. R.: Regurgitation of Fluid from the Bladder to the Kidney During Ureteral Catheterization, Surg. Gynec. Obst. **15**:510, 1912.

15. Kretschmer, H. L.: Cystography, Surg. Gynec. Obst. **22**:209, 1917.

16. Mascagni: Vasorum lymphaticorum corporis humani historica et ichnographia, 1787, p. 45.

17. Teichman, L.: Das Saugadersystem, Leipzig, Wilhelm Engelman, 1861, p. 590.

18. Sappey: Anatomie, physiologie, pathologie des vaisseaux lymphatiques, Paris, V. Masson, 1874.

Krause,[19] in 1876, and Gerata,[20] in 1897, showed by their method of injection that there was a direct communication between the lymphatics of the bladder and those of the lower third of the ureter. Stahr,[21] in 1900, Sakata,[22] in 1903, and Bauereisen,[23] in 1910, were able to demonstrate the lymphatics in the mucous and submucous coats of the ureter, and also a network of perivascular lymphatics in the muscular and fibrous coats. The serial sections, including a section of the bladder and the intramural portion of the ureter, showed a free communication between the lymphatics of the muscular coat of the bladder and that of the ureter. The lymph current of both the bladder and the ureter is from the mucous toward the fibrous coat. The perivascular lymphatics communicate with each other in a transverse as well as in a longitudinal direction, by means of vertical and oblique branches.

Kumita[24] demonstrated in 1909 that the lymphatics of the kidney accompany the blood vessels. They form a capillary network in the cortex surrounding all tubules like the blood capillaries. The lymphatics of the cortex communicate with those of the capsule. This work has been confirmed by Müller;[25] Eisendrath and Schulz,[26] in 1916, Stewart,[27] in 1910, Sugimura,[28] in 1911, Hess,[29] in 1913, Sweet and Stewart,[30] in 1914, and Eisendrath and Kahn,[31] in 1915, experimentally produced ascending infection to the kidney through the lymphatics.

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19. Krause: Handbuch der menschlichen Anatomie, Hanover, Hahn, 1876, vol. 1, p. 5248.

20. Gerata, quoted by Bauereisen (footnote 23).

21. Stahr: Arch. f. Anat. u. Entwcklngsgesch., 1900, p. 41.

22. Sakata: Arch. f. Anat. u. Entwcklngsgesch., 1903, p. 1.

23. Bauereisen, A.: Beitrag zur Frage der aszendierenden Nierentuberkulose, Ztschr. f. gynäk. Urol. **2**:132, 1910; Ein Fall von postoperative entstandener Perinephritis serosa, Ztschr. f. gynäk. Urol. **4**:124, 1913.

24. Kumita: Arch. f. Anat. u. Entwcklngsgesch., 1909, p. 49.

25. Müller, A.: Untersuchungen über die Ausbreitung des entzündlichen Processes im Nierenparenchym bei der aufsteigenden Pyelonephritis, Arch. f. klin. Chir. **97**:14, 1912.

26. Eisendrath, D. N., and Schulz, O. T.: The Path of Involvement in Ascending Infection of the Urinary Tract, J. M. Research **35**:295, 1917.

27. Stewart, L. F.: A Study of Ascending Infection of the Kidney, Univ. Penn. M. Bull. **23**:233, 1910.

28. Sugimura, S.: Ueber die Beteiligung der Ureteren an den akuten Blasentzündungen, Virchows Arch. f. path. Anat. **56**:20, 1911.

29. Hess: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **26**:135, 1913.

30. Sweet, J. E., and Stewart, L. F.: Ascending Infection of the Kidney, Surg. Gynec. Obst. **18**:460, 1914.

31. Eisendrath, D. H., and Kahn, J. V.: Rôle of the Lymphatics in Ascending Renal Infection, J. A. M. A. **66**:561 (Feb. 19) 1916.

Helmholz,[32] in 1922, and David,[33] in 1916, experimentally produced ascending *Bacillus coli* infection of the lumen of the ureter.

Hartzler,[34] in 1925, concluded that ascending infection of the kidney has not been proved.

Sugimura,[29] in 1911, found involvement of the lower end of the ureter in twenty-five cases of cystitis, and demonstrated that the infection extended along the lymphatics.

Carson,[35] in 1925 and 1927, demonstrated cancer cells in the perivascular lymphatics of the ureter, secondary to primary carcinoma of the bladder, prostate and cervix uteri, and in the perivascular lymphatics of the renal pelvis from primary carcinoma of the prostate.

TABLE 1.—*Results Obtained in Series 1*

| | | | | Histologic Observations | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Rabbit | Date of Operation, 1930 | Date Killed, 1930 | Organism Used* | Bladder: Cystitis | Left Ureter | Left Kidney | Right Ureter, 1 cm. Up | Right Ureter, 6 cm. Up 1 cm. Down | Right Kidney | Cultures at Necropsy |
| 1 | 2/10 | 2/12 | S. aureus | Negative | Negative | Negative | Negative | Positive† | Positive | B. coli from heart's blood |
| 2 | 2/12 | 2/25 | S. aureus | Negative | Negative | Negative | Negative | Posi. tive† | Positive | Staphylococcus from bladder; B. coli from heart's blood |
| 3 | 3/ 5 | 3/18 | S. aureus | Negative | Negative | Negative | Negative | Positive† | Positive | Cultures negative |
| 4 | 3/12 | 3/14 | S. aureus | Positive | Negative | Negative | Negative | Positive† | Positive | Staphylococcus from bladder |
| 5 | 3/18 | 4/12 | S. aureus | Positive | Negative | Negative | Negative | Positive† | Positive | Staphylococcus from bladder and right kidney |
| 6 | 3/19 | Died 3/22 | B. coli | Positive | Negative | Negative | Negative | Positive | Positive | B. coli from heart's blood and bladder |

* Two-tenths cubic centimeter of an eighteen hour broth culture.
† Organisms found in perivascular lymphatics.

## EXPERIMENTS

Young adult rabbits were used, with ether anesthesia and aseptic technic. Stock cultures of *Staphylococcus aureus* and *B. coli* were obtained from a human kidney by ureteral catheterization at Columbia Hospital, and the paratyphoid bacilli from Dr. Reith. A fresh eighteen hour broth culture was used in each experiment.

32. Helmholz, H. F.: The Pathological Changes in Experimental Ascending and Hematogenous Pyelitis, J. Urol. **8**:301, 1922.

33. David, V. C.: Ascending Urinary Infection, Surg. Gynec. Obst. **26**:159, 1918.

34. Hartzler, A. E.: Acute Localized Infection of the Kidney, Surg. Gynec. Obst. **40**:247, 1925.

35. Carson, W. J.: Metastatic Carcinoma in the Ureter, Ann. Surg. **82**:142, 1925; **86**:549, 1927.

TABLE 2.—*Results Obtained in Series 2*

| Rabbit | Date of Operation, 1930 | Date Killed, 1930 | Organism Used* | Histologic Observations: Bladder: Cystitis | Left Ureter | Left Kidney | Right Ureter, 2, 4 and 8 cm. Up | Right Kidney | Cultures at Necropsy |
|---|---|---|---|---|---|---|---|---|---|
| 7 | 3/25 | 3/31 | B. coli | Positive | Dilated | Hydronephrosis | Positive | Positive | B. coli from bladder |
| 8 | 3/26 | 4/19 | Para. B.† | Positive | Dilated, marked | Hydronephrosis | Positive | Positive | Paratyphoid bacillus from bladder |
| 9 | 3/28 | 4/ 5 | Para. B. | Positive | Dilated | Hydronephrosis | Positive | Positive | Paratyphoid bacillus from bladder |
| 10 | 4/ 2 | 4/18 | Para. B. | Negative | Dilated, marked | Hydronephrosis | Negative | Negative | B. subtilis from bladder |
| 11 | 4/ 4 | 4/18 | Para. B. | Negative | Dilated | Hydronephrosis | Positive | Positive | Negative |
| 12 | 4/ 8 | 4/24 | Para. B. | Negative | Dilated | Hydronephrosis | Positive | Positive | Paratyphoid bacillus from bladder |

* Two-tenths cubic centimeter of an eighteen hour broth culture.
† Paratyphoid bacillus.

TABLE 3.—*Results Obtained in Series 3**

| Rabbit | Date of Operation, 1930 | Date Killed, 1930 | Histologic Observations: Bladder | Left Ureter, 2, 4 and 8 cm. Up | Left Kidney | Right Ureter, 2, 4 and 8 cm. Up | Right Kidney | Cultures at Necropsy |
|---|---|---|---|---|---|---|---|---|
| 13 | 4/ 9 | 4/24 | Marked cystitis | Positive† | Positive† | Positive | Positive | Negative |
| 14 | 4/ 9 | 4/30 | Moderate cystitis | Positive | Positive | Negative | Negative | Negative |
| 15 | 4/15 | 4/30 | Marked cystitis | Positive† | Positive† | Positive | Positive | Negative |
| 16 | 4/22 | 5/ 5 | Marked cystitis | Negative | Negative | Positive | Positive | Negative |
| 17 | 4/23 | 5/ 2 | Marked cystitis | Negative | Negative | Negative | Negative | Negative |
| 18 | 4/28 | 5/14 | Trigonitis | Negative | Negative | Negative | Negative | Negative |

* One cubic centimeter of an eighteen hour broth culture of paratyphoid bacillus was injected into the bladder.
† Organisms found in the perivascular lymphatics.

*Series 1.*—A midline incision, 4 cm. in length, was made below the umbilicus, the coils of the intestines were packed off with a warm gauze pack, and the right ureter was located as it crossed the iliac artery; at this point the posterior layer of peritoneum was opened and the ureter delivered. A very fine needle was used for injection into the ureteral wall 2 cm. proximal to the bladder, after which mercurochrome-220 soluble was applied to the site of the puncture, the ureter

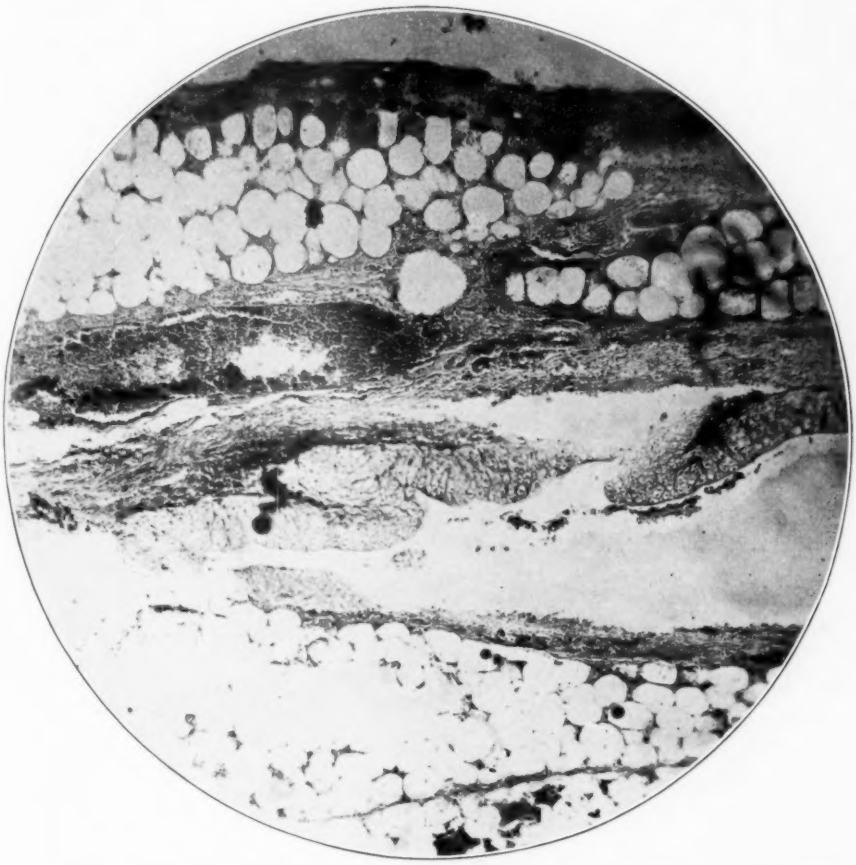

Fig. 1 (rabbit 4).—Photomicrograph of the right ureter, 1 cm. down, showing proliferation of lymphatic endothelium and an infiltration of lymphocytes.

dropped back, the pack removed and the abdomen closed in layers, silk, cotton and collodion dressings being applied.

*Series 2.*—Through a midline incision the left ureter was freed from its peritoneal attachment, from the iliac artery to the bladder, a silk ligature was applied to the ureter at the wall of the bladder, and at a point 1.5 cm. proximal to the bladder, the ureter between these ligatures was then excised for microscopic examination. The right ureter was then located, and the injection was made into

the ureteral wall at its junction with the wall of the bladder. Mercurochrome-220 soluble was applied to the site of the puncture, and the abdomen was closed.

*Series 3.*—A midline incision, 3 cm. in length, was made over the bladder through the skin and linea alba, and the bladder was delivered without opening the peritoneum. Sufficient pressure was applied to the wall of the bladder to force the urine through the urethra, after which 1 cc. of an eighteen hour broth culture was injected into the fundus of the bladder with a fine needle. Mercuro-

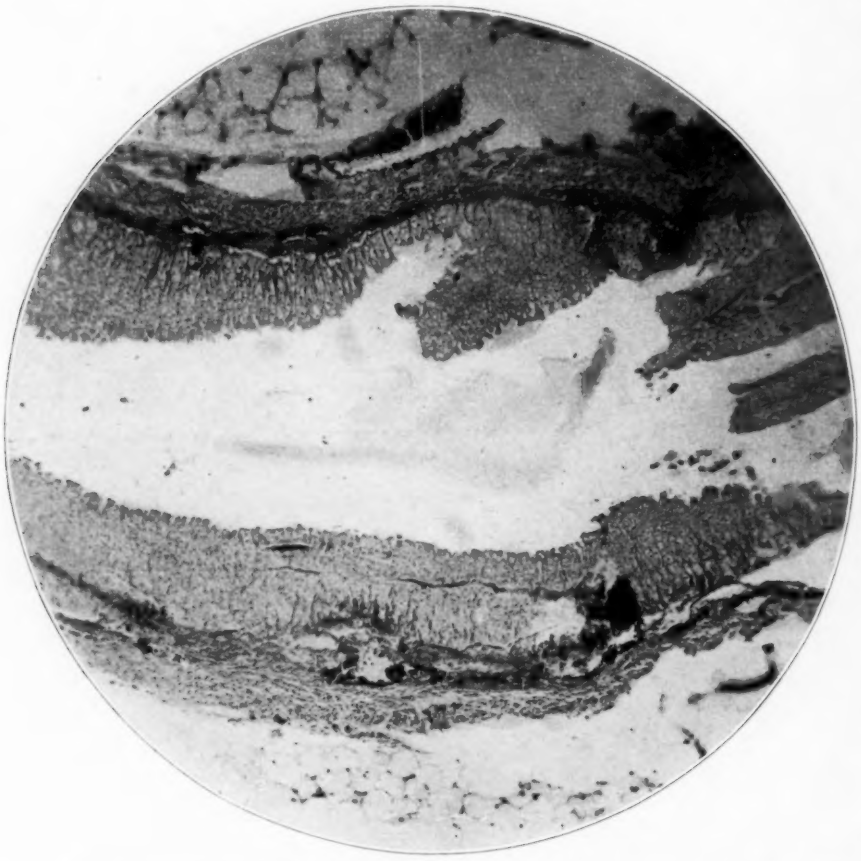

Fig. 2 (rabbit 6).—Photomicrograph of right ureter, 1 cm. down, showing perivascular infiltration of lymphoid cells.

chrome-220 soluble was applied to the site of the puncture, after which the bladder was replaced in the pelvis and the wound closed as in the previous series.

The animals were killed from two to forty-six days after the operation, and an autopsy was performed. Cultures were made from the heart's blood, the peritoneum, each kidney and the bladder.

The tissues were fixed in 10 per cent formaldehyde and embedded in paraffin. Longitudinal sections were cut from each ureter, 1, 2, 4 and 8 cm. above the

bladder, and sections were cut from the bladder and from each kidney to include the pelvis. All were stained with MacCallum tissue stain.

*Histologic Observations.*—In series 1, the right ureter showed the mucosa to be intact above the point of injection, with the epithelial cells distinct in outline, with well stained nuclei. In the submucosa there was an infiltration of lymphocytes, a proliferation of lymphatic endothelium and, in areas, a perivascular lymphoid infiltration. This infiltration extended into the muscular layer and, in

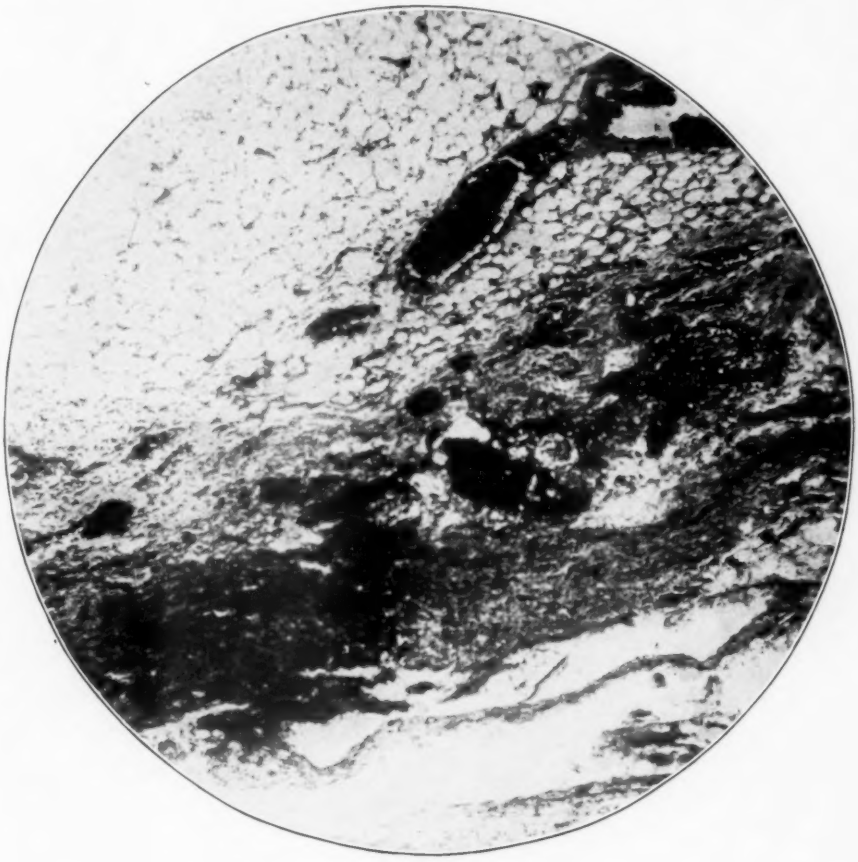

Fig. 3 (rabbit 12).—Photomicrograph of right ureter, 1 cm. down, showing marked proliferation of lymphatic endothelium and an infiltration of lymphocytes.

a few areas, into the adventitia. The inflammatory infiltration followed the lymphatics of the submucosa into the renal pelves, and the kidneys showed a perivascular infiltration of lymphocytes. In the first five experiments, staphylococci were observed in the submucosa. All sections from the left kidney, ureter, bladder and right ureterovesical orifice were normal.

In series 2, the right ureters and kidneys showed essentially the same histologic picture as those in series 1, except that the organisms injected could not

be seen. Sections from the left ureters, removed at operation, were all normal, sections above the ligatures showed a thinning out of the muscular layer, and in rabbits 8 and 10 sections from the left ureters, 4 cm. up, showed a marked proliferation of young connective tissue cells with newly formed blood vessels.

The left kidneys showed a marked dilatation of the tubules with a flattening out of the renal epithelium in areas. Sections from the bladders showed the mucosa to be poorly stained and, in areas, covered with lymphoid cells. In the

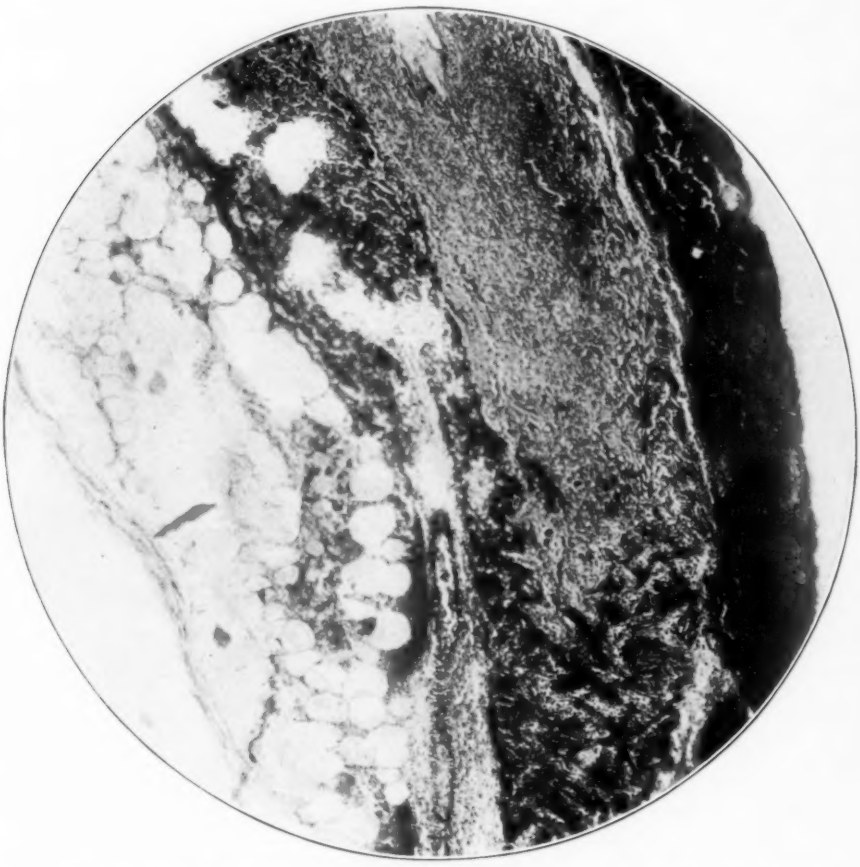

Fig. 4 (rabbit 15).—Photomicrograph of right ureter, 1 cm. up, showing infiltration of lymphoid cells in the submucosa and muscular layers, with a few polymorphonuclear leukocytes.

submucosa marked infiltration of lymphoid cells was seen, with perivascular infiltration in the muscular layer.

In series 3, sections from the bladders showed the mucosa to be absent in areas. In other areas, the epithelial cells were swollen and indistinct in outline, with poorly stained nuclei; large numbers of epithelial cells were fragmented; in areas the mucosa was covered with lymphocytes, polymorphonuclear leukocytes

and fibrin. The submucosa showed a marked infiltration of lymphoid cells, with an occasional polymorphonuclear leukocyte. In the muscular layer a marked perivascular infiltration of lymphocytes was seen. Sections from the right and left ureters in rabbits 13, 14 and 15 and from the right ureter in rabbit 16 showed the mucosa to be well preserved, with a perivascular infiltration of lymphoid cells, which in areas extended into the muscular layer; in rabbits 13 and 15 the organisms were observed in the submucosa.

Fig. 5 (rabbit 15).—Photomicrograph of left ureter, 5 cm. up, showing mucosa well preserved with a perivascular infiltration of lymphoid cells, which infiltrates into the muscular layer.

Sections from the ureters in rabbits 16 (left), 17 and 18 (right and left) showed no changes. Sections from the right and left kidneys in rabbits 13, 14 and 15 and from the right kidney in rabbit 16 showed a perivascular infiltration of lymphoid cells, which extended into the interstitial tissue in areas; sections from the left kidney in rabbit 17 and from the right kidney in rabbit 18 showed no noteworthy changes.

## CONCLUSIONS

Infection produced experimentally in the lower end of the ureter or wall of the bladder has been demonstrated to pass upward through the perivascular lymphatics to the kidneys.

The author was assisted by Dr. T. L. Squier, Director of the Department of Preventive Medicine, and Dr. Allen Reith, Bacteriologist, A. O. Smith Corporation. Mr. Leo Massapust, artist, Marquette University, furnished the photomicrographs.

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# CARCINOMA OF THE BREAST IN THE YOUNG*

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Cancer of the breast in subjects 40 years of age or under is not a rare occurrence. A recent survey of the admissions to the Memorial Hospital from Jan. 1, 1917 to Jan. 1, 1929 showed that 2,663 patients with cancer of the breast had sought admission during this period.[1] The research further revealed that 17.33 per cent (or approximately one sixth) of all patients with cancer of the breast were 39 years or younger. The incidence of mammary cancer in persons in the younger age periods must be borne in mind, otherwise errors in diagnosis will inevitably occur and unfortunate end-results follow.

The material for this paper was furnished by a study of 303 patients admitted to the breast clinic of the Memorial Hospital prior to November, 1926. Radical mastectomy was performed on 191 patients, presenting presumably operable cases at the time of operation. In 44 a radical operation was performed at the Memorial Hospital; in 32 operation was done in other hospitals in New York and the patients were then referred to the breast clinic for postoperative irradiation; 115 patients came to the clinic with recurrent phases of the disease, radical amputation having been done elsewhere. In addition, 52 patients in this series were admitted to the clinic following local mastectomy, local excision or a delayed radical operation after local excision; in many of these patients also the disease was recurrent at the time of admission. The study also includes a survey of 60 patients in the primary inoperable group who had not received surgical treatment, but who were treated by irradiation.

My associates and I have been more impressed year by year with the poor end-results following radical surgical intervention in cases of cancer of the breast in young women; few patients are encountered who survive the three year period. Following operation, the disease is often more rapid in its course, even though examination before operation reveals a well localized process in the breast without apparent involvement of the axillary nodes, recurrences appear earlier and there is usually a fatal termination. This survey was undertaken to determine the exact end-results in this group, and to discover if possible some of the factors contributing to these results.

* Submitted for publication, Nov. 12, 1930.

* From the Breast Clinic of the Memorial Hospital.

1. Pack, George T., and LeFevre, R. G.: The Age and Sex Distribution and Incidence of Neoplastic Diseases at the Memorial Hospital, New York, J. Cancer Research **14**:167, 1930.

FACTORS CONTRIBUTING TO THE END-RESULTS OF OPERATION

*Age.*—Two women, aged 22, were the youngest patients in the entire group. The distribution of patients in five year periods according to age at the time of the inception of the disease is given in table 1.

Mammary cancer is rare in patients 25 years or under, but 3 per cent of our patients under 40 fell within this age period. The occurrence of mammary cancer increases in the older patients, approximately one third of the group being between the ages of 31 and 35, and one half in the five year period from 36 to 40.

TABLE 1.—*Distribution of Patients with Cancer of the Breast According to Age*

| Five Year Age Period | Number of Patients | Percentage |
|---|---|---|
| 21 to 25 | 9 | 3 |
| 26 to 30 | 42 | 14 |
| 31 to 35 | 94 | 31 |
| 36 to 40 | 158 | 52 |
| Total | 303 | 100 |

TABLE 2.—*Previous Lactation*

| | Patients | Percentage |
|---|---|---|
| Yes | 179 | 66 |
| No | 91 | 34 |
| Total | 270 | 100 |

TABLE 3.—*Preoperative Diagnostic Errors*

| | |
|---|---|
| Diagnosis of carcinoma not positively made | 18 |
| Fibro-adenoma | 9 |
| Benign | 5 |
| Abscess | 2 |
| Mastitis | 1 |
| Cyst | 1 |
| Papillary cyst adenoma | 1 |
| Total | 37 |

*Previous Lactation.*—In 270 patients, data were available to determine whether previous lactation had occurred in carcinomatous breasts; the results are given in table 2.

An inspection of this table shows that exactly two thirds of the patients had previously had lactating breasts, whereas one third of the patients had never lactated.

*Diagnosis.*—The diagnosis of cancer of the breast in the young woman is often attended with difficulty. In the cases reported here a preoperative diagnosis of a benign lesion was made thirty-seven times. Table 3 indicates diagnostic errors prior to operation.

If, for the moment, the 60 primary inoperable cases are subtracted from the total number of 303, leaving 243 in which a preoperative

diagnosis was recorded, it will be seen that a correct diagnosis of mammary cancer was not made in 15 per cent of the cases, a definitely higher figure than one obtains when women in the older age groups are studied. In 18 patients the surgeon suspected that he was dealing with mammary cancer, but could not reach a positive diagnosis of malignancy.

In nine patients the preoperative diagnosis was fibro-adenoma, the error in three cases having been made by me. One cannot stress too much the difficulty in differentiating between a fibro-adenoma and true infiltrating carcinoma in the breast of a young woman. Not infrequently, one may encounter a small infiltrating cancer, which on physical examination gives all of the classic symptoms of a fibro-adenoma. There may be no alteration in the position of the nipple, no adherence of skin over the tumor, and the mass itself may appear sharply circumscribed with a definite sense of mobility in the surrounding tissue of the breast. In the light of these experiences, one should always keep in mind that a tumor in a young woman's breast, which is apparently nothing but a simple fibro-adenoma, may really be true infiltrating carcinoma, and therapeutic measures should be outlined with this possibility in view.

In five cases the diagnosis of benign tumor was made, but the exact character of the lesion was not indicated in the records available.

In two patients a diagnosis of abscess of the breast was made, when the patient was really suffering from a rapidly growing inflammatory carcinoma.[2] I have discussed this difficulty in diagnosis in a previous paper. When the surgeon commits this error, and the breast is incised in an attempt to evacuate an abscess, the patient is subjected to serious additional hazard, with the possibility of further dissemination of the disease.

In one patient a diagnosis of papillary cyst adenoma was made, and operation revealed a papillary cyst adenocarcinoma. The differential diagnosis between these two conditions is always difficult whatever the age of the patient, for in both instances one finds a sharply encapsulated tumor with a history of bloody discharge from the nipple, and I know of no method of physical examination which will make this differentiation.

Six patients, comprising 2 per cent of the entire group, were colored. I have noted the comparatively small number of young colored women coming to the clinic suffering from mammary cancer. One may doubt whether this small percentage of colored patients in the series is of significance. Only a complete survey of a large group of colored patients can demonstrate how frequently mammary cancer occurs in young colored women. Such a study can only be made in a hospital to which a large number of colored patients are admitted.

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2. Lee, B. J., and Tannenbaum, N. E.: Inflammatory Carcinoma of the Breast, Surg. Gynec. Obst. **39**:580 (Nov.) 1924.

Only 1 patient of the entire 303 was a man, comprising 0.3 per cent of the total group. It would seem apparent that cancer of the breast is rare in men, 40 years of age or under, a point which should be kept in mind in reaching a diagnosis in tumors of the male breast.

### INFLAMMATORY CARCINOMA OF THE BREAST

In a previous communication, 28 cases of inflammatory carcinoma of the breast were studied. In that series 10, or 36 per cent, occurred in young women, so that our experience thus far at the clinic has shown that approximately one third of the inflammatory carcinomas occur in women, aged 40 years or under. Of the 303 cases in the present series, 26, or 9 per cent of the entire group, were classified as typical examples of inflammatory carcinoma. This is unquestionably the most menacing and rapidly progressive form of mammary cancer. At times the disease resembles an acute infectious process. Physical examination shows

TABLE 4.—*Duration of Life in Young Women with Inflammatory Carcinoma*

| | |
|---|---|
| **Inoperable Cases (When First Seen the Disease Was Widespread and Far Advanced):** | |
| Shortest duration | 4 months |
| Longest duration | 2 years, 3 months |
| Average duration | 1 year |
| **Patients Subjected to Radical Operation:** | |
| Shortest duration | 11 months |
| Longest duration | 2 years, 3 months |
| Average duration | 1 year, 11 months |
| **End-Results:** | |
| Dead | 26 patients |

the affected breast to be definitely larger than normal, with a distinct pinkish blush over it, which may extend well beyond the confines of the breast. The tumor is poorly defined, though usually palpable. The nipple is frequently edematous and retracted, and axillary nodes on the same side are involved early and are usually bulky. Palpation may elicit slight tenderness over the breast, and the temperature taken beneath it may show a rise of from 1 to 1.5 degrees F., as compared to that taken in the mouth. The opposite breast and nodes are also invaded early. We have not seen a case of inflammatory carcinoma of the breast in a young woman which has yielded any but disastrous results following an attempt at radical operation. Recurrence following operation occurs quickly, often immediately, and the whole process frequently spreads over the entire wall of the chest and at times down over the abdomen, around the lateral wall of the chest and onto the back. The only therapy available at the present time which is capable of restraining the growth of these inflammatory carcinomas in young women is adequate irradiation. Table 4 indicates the duration of life in the patients with inflammatory carcinoma.

The histories of several cases are appended which will illustrate the frightfully rapid course of this form of the disease.

## REPORT OF CASES

CASE 1 (no. 174).—N. B., aged 37, married, white, a native of Ireland, had borne four children, two of whom were alive and well. All of the children nursed for a period of approximately one year. Five months before admission to the clinic, the patient fell, striking her right breast against some stiff shrubbery. Following the fall, she suffered from chills and fever and noticed that her right breast was hard, red and swollen. The physician who saw her at that time assured her that she need have no worry concerning the condition of the breast. It, however, remained hard and continued to increase in size. Two months before admission she first noticed a swelling of the right arm which extended down to the hand, and at the same time she became aware of several lumps in the right axilla and right supraclavicular region. For the two months before admission she was unable to abduct the right arm.

Physical examination showed a woman in good general condition. The right breast was enlarged, heavy and thickened throughout, and the skin over it showed a "pigskin" appearance. The nipple was flattened. The skin overlying the breast was irregular and mottled with red patches, some of which were indurated. There was a large mass of nodes in the right axilla, fulness in the right infraclavicular region and enlarged nodes in the right supraclavicular fossa. Examination of the chest at this time showed a few, fine, inconstant, crackling râles over the upper right interscapular region and at the base of the right lung posteriorly, where a slight diminution of breath sounds was noted. There were signs suggestive of metastasis. A roentgenogram of the chest made at the time of admission did not reveal definite evidence of metastasis. A thermometer placed in the right axilla registered 100, and in the left axilla, 98 F.

At the time of admission the patient was suffering considerable pain in the right hand and arm. She was given a cycle of high voltage roentgen treatments, consisting of four treatments over the right breast and drainage areas, the set-up being, time, eighty minutes; milliamperes, 4; spark gap, 90; filters, 0.5 mm. of copper and 1 mm. of aluminum, and focal distance, 50 cm. The patient left the hospital against advice and never returned. A biopsy taken while she was in the hospital showed a cellular, infiltrating carcinoma with considerable fibrosis. The cells were large, probably of the sweat gland type. The follow-up on the patient revealed that she died two months after discharge from the hospital, seven months after the beginning of the symptoms.

CASE 2 (no. 222).—G. M., a colored woman, aged 38, married, was born in the United States. She had borne three children, each of whom she had nursed about seven months. She had never suffered a trauma to the breast. Six months before admission to the clinic she noticed a small lump in the right breast which increased steadily in size until it involved the entire breast. It was unattended by pain until two months before admission, when she began to have pain in and about the right shoulder which increased in severity up to the time of admission. She had complained of a slight cough during the month before her entry into the hospital.

Physical examination showed a woman in fair general condition with apparent emaciation. The right breast was entirely filled with a hard solid tumor. The skin over the breast was thickened and corrugated. The nipple was flattened, and the whole breast was shrunken and fixed to the wall of the chest. A large chain

of nodes extended up to the axilla and through the outer part of the infraclavicular region to the supraclavicular space and neck. There was definite local heat over the breast on palpation, with a reddening of the skin which showed a sharp line of demarcation. Examination of the chest at this time showed dulness at the base of the left lung and a few fine crackling râles at the base of both lungs. A roentgenogram of the chest made at the time of admission showed a thickened pleura and fluid in the left side of the chest, displacing the heart shadow to the right, with further evidence of metastasis in the right side of the chest also.

Treatment by irradiation was begun shortly after admission, three high voltage roentgen treatments being given to the right side of the chest with a set-up of: time, eighty minutes; milliamperes, 4; 0.5 mm. of copper and 1 mm. of aluminum; spark gap, 90 cm. at a focal distance of 50 cm. A month after treatment the

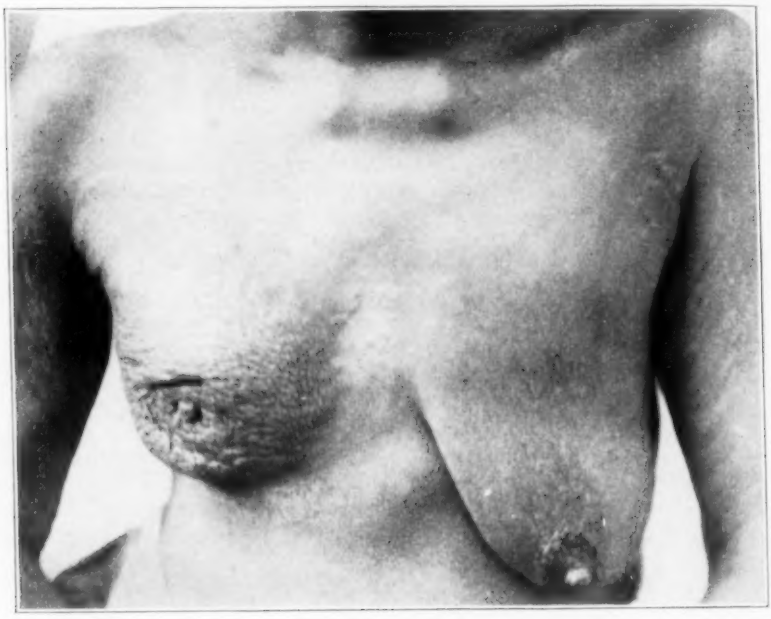

Fig. 1 (case 222).—Primary inoperable carcinoma of the breast, inflammatory type.

patient was somewhat improved with slight regression in the size of the tumor and less pain, but she did not return to the clinic from that time until her death which occurred ten months after admission, and one year and four months from the beginning of symptoms.

CASE 3 (no. 179).—E. C., aged 30, a married white woman, had borne two children, the youngest 19 months old. She had nursed this child for fourteen months, and when the child was weaned (five months before the admission of the patient to our service) she first noticed that the right breast did not return to normal. Her physician advised the use of a breast pump, but there was no change in the size of the breast following this procedure. She consulted a surgeon two months later, who made a diagnosis of abscess of the breast, and a surgical operation was performed with the idea of evacuating an abscess. A few weeks later a

biopsy was made on the small, reddened cutaneous nodule above the breast, and this histologically also proved to be malignant. Six weeks before admission the left breast became infiltrated with tumor tissue. Prior to admission she had received several roentgen treatments to both breasts, with some regression in the size of the tumors.

On admission five months after the beginning of symptoms, there was a diffuse infiltration of both breasts involving all of the organs, with marked reddening over the whole anterior wall of the chest. Nodes were present in both axillae and in the supraclavicular fossae. Examination of the chest strongly suggested metastasis. A poor prognosis was given and a fatal termination predicted within a few months. Roentgen treatment was suggested as the only possible palliation for the disease. The patient returned to her surgeon and received several roentgen

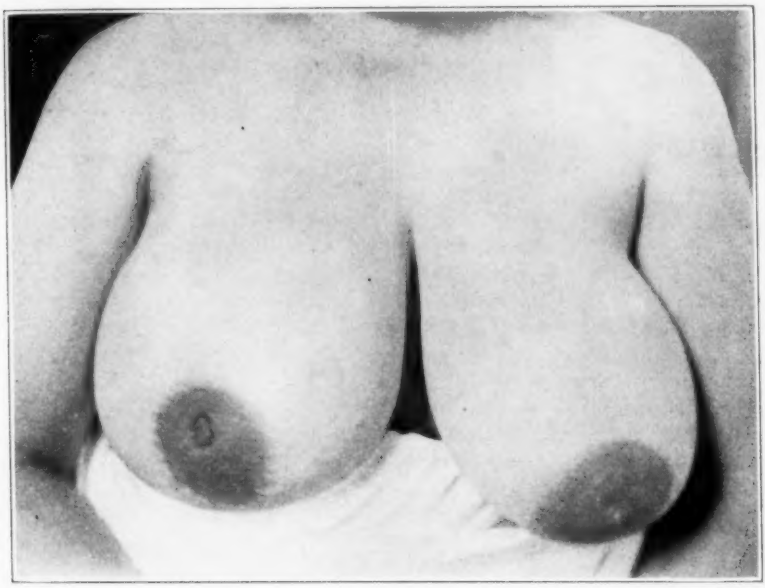

Fig. 2 (case 255).—Primary inoperable carcinoma of the breast, inflammatory type. Note the slightly darker hue of the right breast and adjacent arm.

treatments, but the disease rapidly progressed, and she died four months after admission to our service. The total duration of the disease was nine months.

Case 4 (no. 255).—B. W., aged 33, a married woman, was born in Russia of Hebrew parents. She had borne four children and had nursed each child for one year, using both breasts equally. The last child was born two years before her admission to the Memorial Hospital. No unusual condition had occurred in the breast in connection with lactation. She stated that the right nipple had always been more prominent than the left and that the right breast had always been larger. Two months before admission she first noticed a hardening of the right breast and a retraction of the right nipple. There had been no pain or discharge from the nipples. She thought that she had lost weight recently.

Physical examination showed a woman in good general condition. The right breast was larger than the left, the right nipple was elevated and retracted, with

some fixation of the nipple to the underlying structures. The skin had a definite "pigskin" appearance over the lower segment of the breast. There was a distinct pinkish blush over the whole breast, which ran in oblique fashion upward and inward to the tip of the sternum, with increase of local heat on palpation over this breast. In the middle and outer segment of the breast there was a poorly defined mass 8 by 5 cm. There were several enlarged soft nodes in the right axilla but none in the supraclavicular region. Examination of the chest gave negative results, and the roentgenogram of the lungs did not show definite evidence of metastasis. A diagnosis of inflammatory carcinoma of the breast was made, and treatment by irradiation was begun.

The treatment consisted of three high voltage cycles of four treatments each to the right breast and drainage areas over a period of seven months, the set-up being: time, ten minutes, using the water cooled tube, milliamperes, 30; 6.5 mm. of copper and 1 mm. of aluminum; spark gap, 90 cm., at a focal distance of 50 cm. In addition, the breast itself was also treated with the radium element pack, using 20,000 millicurie hours with exposed area of 70 sq. cm., a filtration of 2 mm. of brass at a distance of 6 cm., the dose being divided through two portals. Following these treatments there was a slight but not marked regression in the tumor. Four months after admission the patient began to complain of pain over the lower portion of the thoracic spine. Although a roentgenogram of the spine was negative, one high voltage roentgen treatment was applied over this area with the set-up described before. Five months after admission the patient had a miscarriage at one month, and a short time later a curettage was performed at another hospital. The following month, on return to the clinic, there had been considerable regression in the size of the tumor in the breast. At the same time a roentgenogram of the chest showed no evidence of metastasis. Four months later, which was one year after the beginning of symptoms, roentgenograms of the pelvis showed extensive metastasis of the osteoplastic type. An irritable cough had developed, and a thickening at the base of the left breast was reported. The disease from this time on progressed steadily, and the patient died one year and two months from the time of admission to the service and one year and four months after the beginning of symptoms.

### PRIMARY INOPERABLE CARCINOMA

Including those with inflammatory carcinoma, sixty patients at the time of their admission to the hospital had advanced primary inoperable cases, in which no thought of radical operation could be entertained. Many of these patients had reached the stage of inoperability a few months from the inception of symptoms, illustrating how rapid had been the course of the disease. They were treated by external irradiation, the high voltage apparatus being generally used. The majority so treated showed some regression in the local disease, but there seemed little doubt that the course of the disease was materially altered by the irradiation. Today we feel certain that mammary cancer must be given adequate irradiation if a considerable degree of restraint in growth is to be obtained by this means, and I know that the irradiation given these patients was inadequate. Others with widespread disease and in poor general condition received little or no irradiation, for treatment would have been futile.

In this group, the shortest duration of life from the beginning of symptoms to death was two and one-half months, another patient survived four months, a third four and one-half months, and but two lived six months. Five patients in whom the course of the disease was less rapid were still living with evidence of disease more than five years after the beginning of symptoms. The average duration of life for the entire sixty was one year and eleven months, while 30 per cent died within one year.

In addition to the case histories of primary inoperable carcinoma of inflammatory type recorded, a few additional histories indicate the rapid course of the disease.

## REPORT OF CASES

CASE 5 (no. 121).—C. L., aged 29, a married Jewess, born in Austria, gave birth to one child four and a half years before admission, which she nursed for thirteen months equally on both breasts. She stated that when she was three months pregnant she had had what was called mastitis in one breast, she thought the left. There had been no trauma to the breast. She said that two weeks before admission she noticed a hardness and tenderness in the left breast. She had had no cough and no loss of weight.

Physical examination showed an apparently healthy white woman in good nutrition. Both breasts were large and pendulous with well formed nipples and areolae. In the left breast there was an irregular, hard, nodular mass, posterior and above the areola, measuring 6 cm. in diameter. Definite retraction of the skin could be made out over the tumor. There was a slight tendency to "pigskin" appearance over the left breast. Sizable firm nodes were palpable in both axillae. General physical examination showed that the mucous membranes were pale. There was deep tenderness over the whole right side of the abdomen, but no tenderness of a specific nor abnormal mass could be palpated, and the edge of the liver could not be felt. Pain was elicited in the region of the first and second lumbar vertebrae on movement of the spine, but no tenderness could be detected here. The x-ray films of the pelvic region showed numerous and extensive areas of metastasis. The patient was admitted to the hospital, and the day after admission complained of pleuritic pain in the right side which subsided in a few days with rest in bed and strapping of the chest. A roentgenogram of the chest made at this time still showed no evidence of metastasis.

The patient was treated with radium element pack over the breast and drainage areas, using 20,000 millicurie hours over the left breast at 6 cm. with 1.5 mm. of brass and 0.35 mm. of platinum filter. Sixteen thousand millicurie hours of treatment were given in a similar manner over the left axilla, and 8,000 millicurie hours over the left supraclavicular region. In addition, 20,000 millicurie hours were given over the lumbar spine and a high voltage roentgen cycle of four treatments was applied to the pelvis using 185 kilowatts, 0.05 mm. of copper and 1 mm. of aluminum filter, target skin distance of 50 cm., over a field of 8 by 10 cm., 30 milliamperes of current with twelve minute exposures.

A blood count made as the treatment was finished showed: hemoglobin, 60 per cent, with red cells, 3,064,000; white cells, 3,400; polymorphonuclears, 57 per cent; large lymphocytes, 10; small lymphocytes, 15; transitionals, 14; eosinophils, 3, and basophil, 1. Three and one-half weeks later the hemoglobin had dropped to 35 per cent, the red cells to 1,856,000 and the white cells to 2,600 with the differential

count not significantly altered. Unfortunately a blood count was not made on admission, so that it is impossible to state how much of the anemia was due to the disease and how much to the irradiation, but it is probable that both contributed. The patient left the hospital, but never returned. The disease progressed with alarming rapidity, and she died four months after her admission, and four and a half months after the beginning of the symptoms.

As one reviews this case, it seems evident that the irradiation applied did not stay the course of the disease, and it seems not improbable that it may have hastened the death of the patient. Moreover, the degree of response of the tumor in the breast to irradiation showed that the neoplasm was a radioresistant type in which irradiation is of comparatively little value.

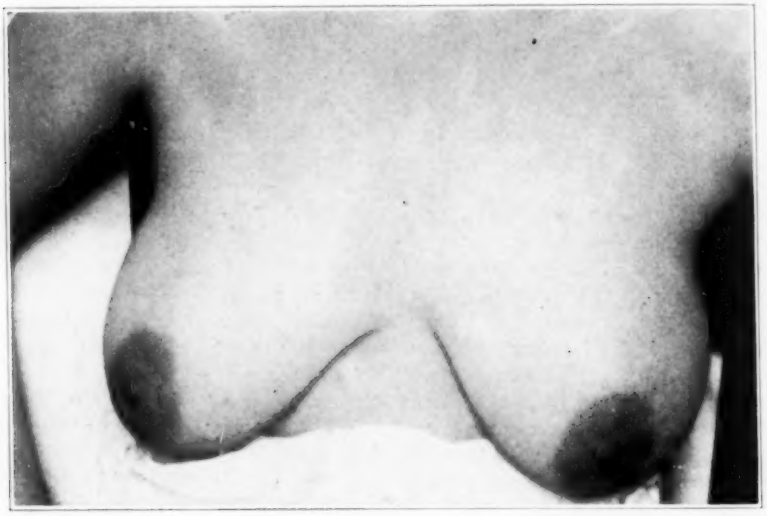

Fig. 3 (case 121).—Primary inoperable carcinoma of the breast. The left breast is slightly larger than the right. Few local symptoms were evident on inspection, although the patient at this time was suffering from widespread metastasis.

Case 6 (no. 225).—M. N., aged 40, a white woman, born in the United States, single, had had no history of trauma to the present or any abnormal mammary history. Nine months before admission she noticed a lump the size of a marble in the center of the left breast beneath the nipple, unattended by pain or tenderness.

Physical examination showed a woman in good nutrition. The left breast was almost completely occupied by a mass 13 by 14 cm. with retraction of the nipple and fixation of the skin over the mass and an area of ulceration 2 cm. in diameter over the tumor which was fixed to underlying structures. One advertent node was palpable in the left axilla. The supraclavicular region was normal. Examination of the chest showed diminished resonance and decreased breath sounds from the third rib to the apex of the left lung, but no râles could be heard. Close to the midsternal line opposite the third rib were three shotty nodules in the skin.

The discharge from the ulcerating mass was foul and a local mastectomy was deemed advisable to free the patient from her disagreeable condition.

A local mastectomy was done in which a wide elliptical incision was made, and the whole wound was left open save for one or two traction sutures at its extremities. At operation it was found that the muscles were extensively involved, and the incision passed through carcinomatous tissue at the lower edge of the axilla. An attempt was made to close in the axilla by sutures. The histologic report of the tissue, made by Dr. Ewing, showed that the breast was large, firm and fat. The nipple and skin for a zone of 5 cm. was excoriated, scaling and indurated, and for a zone of 8 cm., the skin was indurated and thickened as by infiltrating carcinoma. The area around the nipple was enlarged, and it fused with the underlying tissues into a dense, inelastic cone-shaped mass, the base breaking up into a series of isolated cicatricial areas throughout the larger area of the breast. Firm areas appeared on the borders of the breast. None of the areas showed chalky points, but the diagnosis of carcinoma in the nipple and other areas was based on the induration. Three considerable layers of muscle were quite firmly attached to the under surface of the breast, but no definite invasion of the process into the muscle could be seen. The microscopic report revealed: infiltrating carcinoma, large opaque cells throughout all of the suspicious areas, infiltration of the muscles, and wide infiltration of the skin. Three weeks later the granulating surface was grafted by the Thiersch method, the grafts being removed from the left thigh. The patient left the hospital and did not return for postoperative irradiation. The disease progressed rapidly, and she died four months after the palliative mastectomy, with evidence of advanced disseminating disease.

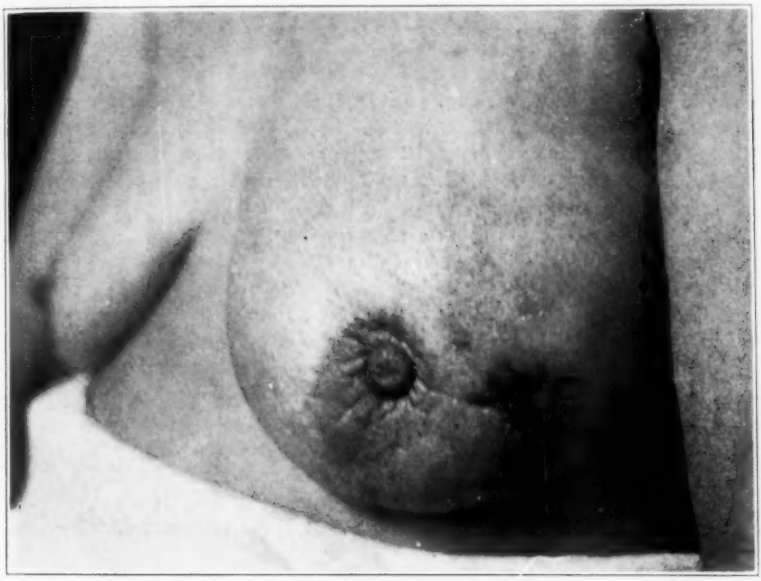

Fig. 4 (case 225).—Primary inoperable cancer of the breast. The left breast was completely occupied by tumor.

In reviewing this case one feels certain that the effort to rid the patient of a foul ulcerating mammary cancer by palliative mastectomy was unwise and that some form of palliative irradiation might have carried her along equally as well or better than did the attempt at operation. If palliative mastectomy is to be undertaken in extensive ulcerating carcinoma one must be reasonably sure that the line of incision between the tail of the breast and the axilla will not pass through actively growing carcinoma, which was unfortunately the case in this patient.

CASE 7 (no. 251).—A. T., aged 39, a married, Jewish woman, born in Russia, had had five children, the first child being born thirteen years and the last nine years before the patient's admission to the Memorial Hospital. Lactation in all instances lasted about ten months with no mammary complication. There had been no history of trauma. Two months before admission the patient noticed a hard lump about the size of an egg in the left breast, which had steadily increased in size up to the time of admission. During this period she was conscious of a drawing sensation in and about the breast. On her own initiative she had applied salves and heat which she thought had caused some regression in the size of the tumor but had resulted in a blistering and reddening of the skin.

Examination on admission showed the patient to be in fair general nutrition. In the middle outer portion of the left breast was a poorly defined area of thickening 5 by 7 by 3 cm. There was moderate retraction of the nipple with some edema about it, and the nipple was fixed to the underlying breast tissue. Fixation of the skin was found over the tumor with an orange skin appearance over the outer and lower segment of the breast. There were several superficial blisters overlying the breast itself which was movable over deeper structures. A mass of axillary nodes 2 by 2½ cm. was palpable high in the left axilla. A roentgenogram of the chest showed no evidence of metastasis. There was some discussion in the breast clinic as to the operability of the case, but I felt that it was inoperable because of the high axillary nodes. Treatment was therefore begun immediately, and consisted of three low voltage roentgen cycles over the left breast and drainage areas with the following set-up: time, twenty-five minutes; milliamperes, 4; filters, 6.25 mm. of copper; spark gap, 10, and focal distance, 15. The last cycle was finished in March, 1925. Seven months after admission a small left supraclavicular node was palpable, and a month later signs of metastasis were evident in the chest. The following month (nine months after admission) the mass in the breast had increased considerably in size and several nodules had appeared in the skin above the breast. A roentgenogram of the chest made at this time gave evidence of metastasis in both lungs. The patient's general condition was decidedly poorer than at the time of admission. One of the skin nodules removed was reported as infiltrating fibrocarcinoma. The patient finally left the Memorial Hospital, being transferred to another hospital where she died eleven months after admission to our service and one year and one month from the beginning of the symptoms. The disease had extended to the liver. One liter of fluid had been removed from the right side of the chest and there was extreme dyspnea before death.

As one reviews this case one may perhaps question the wisdom of having withheld radical operation when any question existed as to operability. My own conviction is, however, that in such a rapidly

progressive disease with high axillary nodes radical surgical intervention two months after the tumor was noted would have been of no avail.

*Segment of the Breast Primarily Involved.*—In 140 cases the left breast was the seat of disease; in 158 cases the right, and in 5 instances both breasts were involved. Dependable data are available in 140 cases concerning the site of the primary disease in the breast.

Figure 5 indicates the percentage of occurrences in various segments of the breast.

The most frequent site of the primary disease in carcinoma of the breast is the outer upper quadrant, 28 per cent occurring in this region,

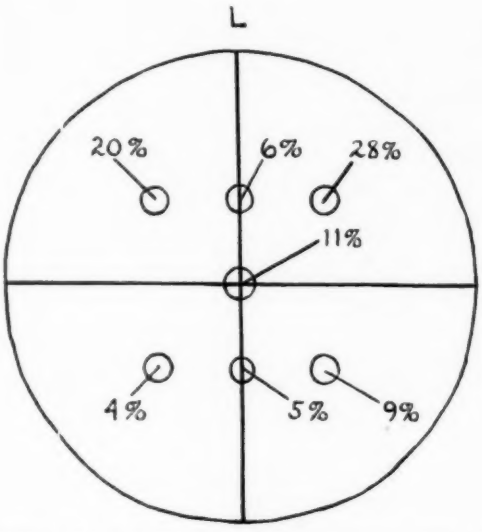


Fig. 5.—Segments of the breast in which disease occurred. The entire breast was affected in 17 per cent of the cases.

approximately one fourth of the entire group. If interference with drainage of the breast can be assigned as a cause for carcinoma, one would expect to find the primary disease more often in the upper outer quadrant, which extends far out toward the axilla, and drainage from this particular area is less effective than that from any other segment. In 20 per cent of the patients, the primary focus was in the upper inner quadrant. The most significant observation in these young women was a diffuse thickening of the whole breast as the initial symptom in 17 per cent of the cases, or approximately one sixth of the entire number. The primary focus was located with about equal frequency in the midportion of the breast and the lower outer quadrant.

Opinion has been unanimous that carcinoma of the breast involving the upper inner quadrant is more prone to furnish early metastasis in the chest than when the tumor invades other segments of the breast.

Figure 6 indicates the segments of the breast in which early pulmonary metastases are most prone to develop, and gives the percentage figures of occurrences in connection with each segment.

In the twenty-eight cases in which the upper inner quadrant of the breast was the primary site of disease, 21 per cent showed pulmonary metastasis as the first apparent extension of the disease, but 31 per cent of the sixteen patients in whom the middle segment of the breast was first involved showed the initial extension of the disease to the cavity of the chest.

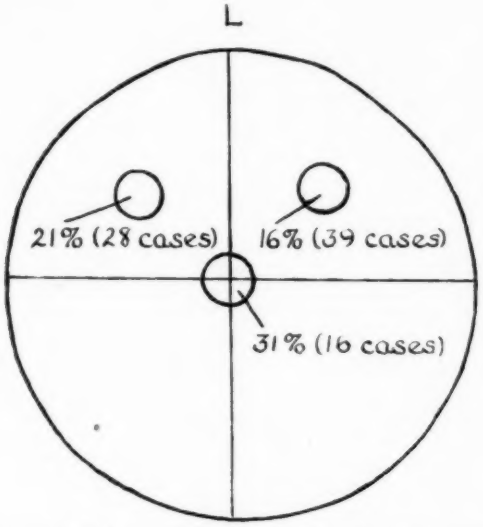


Fig. 6.—Percentage of pulmonary metastasis in various segments of the breast.

The groups of cases giving these percentages are not sufficiently large from which to draw too definite conclusions, but the menace of involvement of the upper inner quadrant of the breast, with the possibility of an extension of the disease to the intercostal lymphatics, is no more menacing, if as menacing, as when the middle segment of the breast is the site of disease.

### PRIMARY OPERABLE CARCINOMA

Patients with primary operable cases, 243 in number, came to the clinic under one of four categories: (1) 44 patients with a primary operable setting, who were subjected to radical amputation at the Memorial Hospital; (2) 32 patients who received radical amputation in other hospitals in New York and were then referred to the clinic

for postoperative irradiation; (3) 115 patients who underwent radical amputation elsewhere, entering the clinic in recurrent phases of the disease, and (4) 52 patients with an operable setting who received some type of operation less extensive than radical amputation.

It is well to bear in mind that the 44 patients treated at the Memorial Hospital received uniformly a preoperative cycle of roentgen treatments before surgical intervention was attempted, and all received postoperative irradiation. The patients referred to the Memorial Hospital for irradiation after radical amputation elsewhere, received postoperative irradiation, no preoperative irradiation having been given. The 115 patients admitted in recurrent phases of the disease received neither preoperative nor postoperative irradiation, but were treated only for recurrent manifestations of the disease by irradiation methods.

Table 5 indicates the three year results following radical mastectomy in the three groups of patients mentioned. Figure 7 gives the percentage of patients alive and well at three month intervals during the entire three years. A study of table 5 suggests the conclusion that the

TABLE 5.—*Three Year Results Following Radical Mastectomy*

| | Alive and Well | Per Cent | Alive and Recurrent | Dead | Total |
|---|---|---|---|---|---|
| Memorial Hospital patients | 16 | 36 | 8 | 20 | 44 |
| Referred for postoperative irradiation | 6 | 20 | 9 | 17 | 32 |
| Recurrent on admission | 8 | 7 | 31 | 76 | 115 |
| Total | 30 | 16 | 48 | 113 | 191 |

preoperative irradiation applied to the patients treated at the Memorial Hospital resulted in a higher percentage of success than did the deferred irradiation, for sixteen were alive and well at the end of three years. The fact that the criteria for the selection of patients for radical operation may vary considerably in the minds of different surgeons must, however, be taken into account. It seems fair to state that the criteria of operability are more sharply drawn at the Memorial Hospital than at other surgical clinics. There is, perhaps, a stronger tendency to scrutinize the patients carefully to be sure that a good operable setting exists. One might fairly assume that the better percentage in the group from the Memorial Hospital may be accounted for as much by the careful selection of cases as by the use of the preoperative cycle of roentgen treatments. Moreover, recent investigations carried on at the hospital strongly suggest that the preoperative cycle used as a measure of routine during the past ten years may be somewhat less effective than has been believed.

There is, however, no question that mammary cancer of radiosensitive type is definitely affected by the use of preoperative irradiation, and this evidence is found clinically in the regression in the size of the

tumor, and in the pathologic laboratory where histologic evidence abundantly demonstrates pronounced changes in the tissue in the irradiated tumors. These changes are more marked if a period of from three to five weeks is permitted to elapse before the radical amputation is undertaken. Further, inspection of table 5 shows that patients from the Memorial Hospital and those referred for postoperative irradiation give strikingly higher percentage figures for the three year results than do the patients admitted in recurrent phases of the disease. These better percentages may be explained on several grounds. Most of the patients referred for irradiation came from well organized surgical

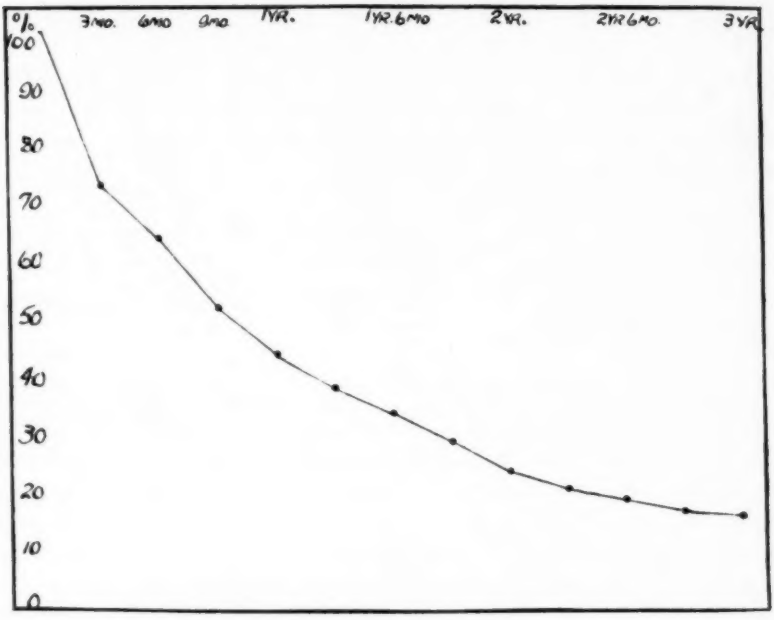


Fig. 7.—Percentage of 191 patients alive and well at intervals of three months for three years following radical mastectomy.

clinics in the city, where careful scrutiny of the patient is made and where the best type of surgery is done. Both of the first two groups, namely, the patients from the Memorial Hospital and those referred for postoperative irradiation, received radiation therapy following radical amputation, whereas those in recurrent phases of the disease did not. There seems little question that postoperative irradiation properly planned and efficiently given is of service in preventing recurrence and in causing the restraint of growth in tumor cells which may be left behind following surgical intervention. But, one factor must not be lost sight of, namely, that the surgeons whose patients finally found

their way into the Memorial Hospital clinic in recurrent phases of the disease undoubtedly had a certain number in whom the end-results were more favorable and who may have survived the three year period without evidence of recurrence. Without these additional facts from various surgeons, it is apparent that the figures for the recurrent group do not fairly represent the cross-section of the end-results in this group. With this in mind, the figure of 16 per cent for the three year results of radical amputation of mammary cancer in young patients is probably a lower figure than the correct one. The total of the Memorial Hospital patients and those referred for irradiation is seventy-six, twenty-two of whom were alive and well at the end of three years, a percentage figure of 30 per cent, which, we believe, probably more nearly represents the end-results to be expected.

Table 6 illustrates the three year results in the 191 patients subjected to radical amputation, when they are divided into five year age groups.

From a statistical standpoint, the number of patients occurring in the age groups of from 21 to 25 and from 26 to 30 years is too small

TABLE 6.—*Three Year Results After Radical Mastectomy*

| Age Period | Number of Patients | Percentage Alive and Well |
|---|---|---|
| 21 to 25 | 6 | 17 |
| 26 to 30 | 24 | 17 |
| 31 to 35 | 58 | 12 |
| 36 to 40 | 103 | 17 |
| Total | 191 | |

to compare with the other two groups. The fifty-eight patients in the age group from 31 to 35 years and the significant facts that have been discovered explain the lower percentage of survivals in the age group from 31 to 35 years.

## FACTORS INFLUENCING THREE YEAR END-RESULTS

*Influence of Axillary Metastasis in Three Year End-Results.*—Dependable data were available in sixty patients on the presence or absence of metastasis in the axillary nodes at the time of radical amputation. Of this number, axillary metastasis had been proved in forty-two patients at the time of operation, and at the end of three years but 10 per cent were alive and well, with no evidence of disease.

In the eighteen patients without involvement of the axillary lymph nodes, 67 per cent were alive and well three years following radical operation. These figures closely follow surgical experience with carcinoma of the breast without respect to age periods. In the patients in whom the nodes were involved, the average duration of life after operation was two years and six months, whereas those with no invasion of

the axilla gave an average duration of life after operation of five years and three months.

*Influence of Lactating Breasts in Three-Year End-Results.*—Experience at the Memorial Hospital has impressed us with the added menace to the patient with mammary carcinoma of a lactating breast. We have felt so certain of the seriousness of this clinical picture that in the presence of pregnancy we have uniformly advised therapeutic abortion before any attempt was made to deal surgically with the carcinoma of the breast. The present study confirms this conviction. In the series of 191 operable cases in which radical intervention was employed, a lactating breast was coexistent with the mammary carcinoma in 25. The end-results for this group of 25 women showed but 8 per cent alive and well without disease at the end of three years. When this figure is compared with the one already given, namely, 16 per cent for the entire group, it would seem fair to conclude that lactation coexistent

TABLE 7.—*Results of Limited Surgical Intervention in Operable Cases After Three Years*

| Type of Operation | Number of Patients | Percentage Alive and Well |
|---|---|---|
| Limited radical | 5 | 0 |
| Local mastectomy | 17 | 29 |
| Local excision | 18 | 22 |
| Local excision and radical amputation after 2 weeks or more | 12 | 12 |

with mammary cancer suggests a distinctly more menacing clinical picture and a poorer prognosis for the patient.

*Three Year Results of Limited Surgical Intervention in Primary Operable Cases.*—Fifty-two patients presenting a picture favorable for primary operation were subjected to surgical procedures less extensive than radical amputation. In some of these the breast was removed, and an incomplete axillary dissection done without any attempt to remove the pectoral muscles. Surgical intervention of this type, for want of a better name, we have called "limited radical." Other patients underwent local mastectomy only, a local excision of the tumor itself or a local excision, radical intervention being done more than two weeks after the preliminary operation. Table 7 gives the results in this group of cases at the end of three years.

None of the patients subjected to a "limited radical" operation survived the three year period. The reasons for employing such a surgical procedure is not always apparent. It seems probable that either poor surgical judgment determined the type of operation to be performed or that the clinical setting was too advanced to expect much from radical surgical intervention. Whatever the reasons for adopting this method, the end-results demonstrate that "limited radical" operations are unwise

in dealing with mammary cancer. Local mastectomy alone was performed 17 times, with a much higher percentage of patients alive and well than that obtained for the 191 patients subjected to radical amputation, but lower than that, 36 per cent, for the patients from the Memorial Hospital. Local mastectomy was chosen, apparently, because of the clinical setting, for in many instances a positive diagnosis of cancer was not made prior to the time of operation. Moreover, many of these patients had no palpable axillary nodes, which may have influenced the surgeon in his judgment toward local mastectomy; it is also possible that many of these cases were of lower grades of malignancy. In general, the procedure is to be condemned as an alternative for radical surgical intervention.

Local excision was performed in eighteen cases, and there is little doubt that in most of them the preoperative diagnosis was that of benign tumor. The fact that 22 per cent of the patients survived the three year period suggests that many of the tumors were of a low grade of malignancy.

But 12 per cent of the twelve patients in whom local excision was followed by radical amputation after two weeks survived the three year period. The experience of many surgeons, especially that of Peck and White,[3] has strongly suggested that local excision followed shortly by radical mastectomy yields as good end-results as radical amputation alone, but a delay in performing the latter adds to the patient's hazards.

The results of these types of limited surgical intervention in the fifty-two cases have been recorded for completeness, but any surgical procedure less than a radical amputation in a group of younger women should be condenmed and considered poor surgical practice.

### RECURRENCE AFTER RADICAL MASTECTOMY

A study of the rapidity of recurrence shows several interesting facts. Table 8 indicates the number of patients of the entire series of 191 in whom the disease recurred after a postoperative interval of three months and one year.

Inspection of table 8 shows the rapidity of recurrence in all of the groups but especially in those coming to the clinic in recurrent phases of the disease. In more than one third of these patients the disease recurred within three months, and in approximately two thirds it had recurred within the first postoperative year. The percentages of recurrences in the Memorial Hospital patients and in those referred to us for postoperative irradiation are fairly comparable and should represent what one might reasonably expect to be the result of radical amputation

3. Peck, C. H., and White, W. C.: Tumors of the Breast, Benign and Malignant, Ann. Surg. **75**:641, 1922.

in well selected operable cases in young women. When the entire group of 191 patients is considered, it will be seen that the disease recurred in a little over one fourth of the patients within the first three months and in exactly one half within the first year.

Table 9 represents the result of the analysis of all the cases recurring within three months.

The inevitable conclusion to be drawn from a study of these cases of rapid recurrence is that either the patients were unsuited for radical surgical intervention, that poor surgical technic was employed in the radical amputation, or that both factors combined to give the poor end-result.

One should scrutinize most carefully the whole clinical setting in a case of mammary cancer in a young woman, and only after most careful physical examination should the surgeon reach a decision as to the favorable condition of the patient for operation.

TABLE 8.—*Recurrence of Disease After Radical Amputation*

| | In Three Months | | In One Year | |
|---|---|---|---|---|
| | Patients | Per Cent | Patients | Per Cent |
| Memorial Hospital patients | 5 | 11 | 15 | 33 |
| Referred for postoperative irradiation | 4 | 13 | 9 | 28 |
| Recurrent on admission | 42 | 36 | 72 | 63 |
| Total | 51 | 27 | 96 | 50 |

TABLE 9.—*Rapid Recurrence After Radical Mastectomy*

| | |
|---|---|
| Immediate | 5 |
| Within 1 month | 17 |
| Within 2 months | 13 |
| Within 3 months | 16 |
| Total | 51 (27%) |

Concerning the surgical technic, one is impressed with the tendency to perform radical amputation with too much speed and too little care, the operation often being a traumatizing procedure. Unless every detail of surgical technic is carefully thought out and put into practice, early recurrence will surely follow, and the study of the present series of cases proves that the hazard of early recurrence is present to a much larger degree in young than it is in older women.

The following history indicates the lack of wisdom in operating on a younger woman in whom the condition was clearly inoperable from the outset.

CASE 8 (no. 250).—S. A., aged 40, a white woman, married, was born in Poland. She had had seven previous lactations, the first seventeen years and the last one year before admission. She usually nursed her babies for eighteen months. Two weeks before she entered the Memorial Hospital she noticed that the whole right

breast was becoming swollen. Shortly afterward the breast felt hard. The swelling increased rapidly, and at this time the patient noticed sticking pains and a burning sensation in the breast.

Physical examination showed the patient to be in fair general nutrition. The entire right breast was enlarged and completely occupied by a tumor. There was marked retraction of the nipple, which was edematous, and the lower segment of the breast showed a definite pigskin appearance. There was fixation of the skin to the underlying mammary tissue, and the surface of the breast was red, with irregular multiple nodules over it. There was a large chain of hard nodes in the right axilla and a questionable node in the right supraclavicular region. A roentgenogram of the chest was made and was negative for metastasis. A diagnosis of inoperable carcinoma was made, and it was decided that the patient should be treated entirely by irradiation. One high voltage cycle of roentgen ray was given

Fig. 8 (case 260).—Photograph shows extensive pigskin appearance of the right breast.

over the right breast and drainage areas with the following set-up: time, six minutes; milliamperes, 4; filter, 0.5 mm. of copper; spark gap, 90 cm., at a focal distance of 50 cm. The patient left the clinic, and two months later a radical amputation was performed.

The pathologic report of the tissue removed showed the case to be one of infiltrating carcinoma simplex, with large opaque cells. Two months after the operation a letter from the patient stated that she was "home now, but not doing the way I expected to be. I believe it's starting in my other breast now, because today it's all inflamed and very feverish. Have a pain in it and in the pit of my arm."

During this time she was still going to the hospital for dressings, the incision not having healed. Through the wound of operation a fungating tumor formed, and, although some attempt was made to control the disease by palliative irradiation, the whole process was rapidly progressive, with wide dissemination, and the patient died five months after the operation and seven months after the beginning of symptoms.

One hundred and forty-three patients are available in whom five year end-results may be tabulated. Figure 9 gives the percentage of those alive and well at intervals of six months during the entire five years.

PATHOLOGIC REPORT

Gross material, microscopic slides or histologic reports from other hospitals were obtained in 169 of 303 patients.

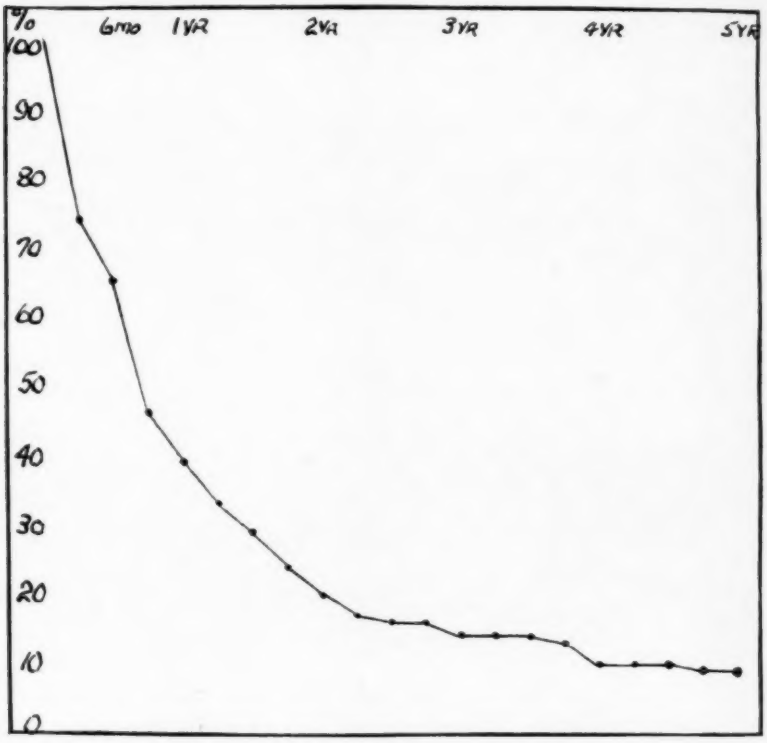


Fig. 9.—Percentage of 143 patients alive and well at the end of five years following radical mastectomy.

From the Memorial Hospital, tissue was available for study in all of the forty-four primary operable cases and in twenty-eight of the sixty primary inoperable cases. In the group referred to us by other New York hospitals for postoperative irradiation, slides were available in the majority of instances, and in practically all of the other cases of this group, histologic reports were sent to the clinic. Few microscopic slides were obtained of the cases in the recurrent group, but in approximately one half of these, histologic reports were obtained.

A wide variation exists in the minds of different pathologists as to the histologic types of mammary cancer. Therefore, a tabulation of these 169 patients would appear to us to be of little value from the standpoint of accurate information on the histology of this disease, so we have excluded it from this report.

Tissue for histologic study in the laboratory at the Memorial Hospital was available in seventy of the patients. In eight instances the histologic material obtained from sources outside the hospital was of such a character that it was impossible to determine the type of the disease. Table 10 indicates the types encountered in the remaining sixty-two patients. Inspection of this table shows that forty-two cases (or slightly more than two thirds) were of the duct carcinoma type; ten of these were of the small cell variety, which has been considered in the laboratory a particularly menacing form of the disease with a

TABLE 10.—*Histologic Types of Sixty-Two Patients*

| | Number of Patients | Total |
|---|---|---|
| Adenocarcinoma | | |
| Bulky adenocarcinoma | 12 | |
| Gelatinous adenocarcinoma | 2 | |
| Papillary adenocarcinoma | 2 | 16 |
| Duct carcinoma | | |
| Small cell duct carcinoma | 10 | |
| Infiltrating duct carcinoma | 27 | |
| Large cell duct carcinoma | 1 | |
| Duct carcinoma, sweat gland type | 2 | |
| Intraductal papillary carcinoma | 2 | 42 |
| Infiltrating tubular carcinoma | 3 | 3 |
| Carcinoma simplex | 1 | 1 |

tendency to disseminate early and widely; twenty-seven others were classified as infiltrating duct carcinoma. This form of the disease, although less active than the small cell type, is nevertheless serious. Of the sixteen adenocarcinomas, twelve were classified as of the bulky adenocarcinoma type, which early in its course is not a highly malignant tumor of the breast; later, as the disease progresses and nodes become involved, it shows infiltrative qualities, and in this stage presents a serious form of the disease. There were but two cases of gelatinous adenocarcinoma, a tumor generally recognized as of low grade malignancy. Two cases of papillary adenocarcinoma and two additional ones of intraductal papillary carcinoma were also encountered, and both of these lesions are relatively benign. The histologic survey demonstrated that but six cases of the entire group were of low grade malignancy.

Histologic grading was done in forty-three of the patients, placing six in grade 1, twenty-six in grade 2 and eleven in grade 3. The thirty-seven patients falling into grades 2 and 3 constituted 86 per cent of the forty-three cases studied.

In this series fifty-two of the histologic slides studied with respect to radiosensitivity showed that thirty-six could be classified as radioresistant and but sixteen as radiosensitive. An attempt to determine the quality of radiosensitivity or radioresistance in mammary cancer is attended with considerable difficulty. It seems probable that the reaction of tumor tissue to irradiation depends as much on such factors as the supply and abundance of the blood and the character of the stroma as on the inherent qualities in the cancer cell itself. The small cell duct carcinomas are generally regarded as radiosensitive, as are also some of the papillary adenocarcinomas. If the tumor is highly cellular, with little stroma, one is inclined to consider it as sensitive to irradiation. One cannot conclude that a high degree of malignancy is always associated with radiosensitivity, for some of the highly malignant forms of mammary cancer are comparatively radioresistant.

Histologic studies were made of a similar number of patients in the age group of 60 years and over, in order to determine if any marked difference existed in the histologic appearance as compared with that of the younger patients. This study revealed that more tumors of an adenocarcinomatous type and fewer instances of small cell duct carcinoma were apt to be encountered in the older women. No marked difference could be discovered in these two divergent age groups with respect to the quality of radiosensitivity.

## TREATMENT

The first step in the appropriate treatment of a young woman suffering from a tumor of the breast is a complete physical examination to establish a correct preoperative diagnosis. If a diagnosis of mammary cancer is made, or is strongly suspected, roentgenograms of the chest and osseous system should be studied for metastases. If the breast is largely occupied by tumor tissue, if the axillary nodes are extensively invaded or if there are one or more cutaneous nodules overlying the tumor in the breast, the case should be considered inoperable. On the other hand, if there is a small or moderate-sized tumor in the breast, without invasion of the axillary nodes or with but one or two palpable nodes, radical amputation would seem the proper course to follow. Before surgical intervention is undertaken, the patient should be treated adequately by irradiation, a cycle of high voltage roentgen treatments being given over the breast and drainage areas. If the tumor is radiosensitive, regression in size will follow within three or four

weeks. No benign tumor of the mammary gland responds in this way to irradiation. If the tumor is of radioresistant type, the degree of regression will be less marked or there may be no diminution in size.

Recent investigations at the Memorial Hospital have shown that devitalization of mammary cancer requires the equivalent of ten full erythema doses that can be delivered by high voltage roentgen rays to the most distant part of the tumor. During the past few months, I have attempted to deliver this dose by supplementing the high voltage roentgen cycle with interstitial radiation, furnished by the insertion of gold radon seeds directly into the mass. The tumors are carefully measured and their exact size and shape plotted. Through the cooperation of the physics department, we have been able to obtain information as to the exact amount of gold radon seeds which must be implanted to bring the total dosage up to an equivalent of ten erythema doses. This amount is apparently sufficient to devitalize the most radioresistant cancer of the breast. The axilla is treated in a similar manner. Radical amputation is performed from four to five weeks after the insertion of the radium, and histologic studies revealed in many instances almost complete devitalization of the tumor. Time will show whether the end-results following this procedure justify the method.

Following the operation, postoperative irradiation is for the present being withheld, because it seems wise to determine the adequacy of preoperative irradiation.

A similar procedure is followed in the patients in whom the disease has passed beyond the stage of operability. If an ulcerating mass is present, a palliative mastectomy is often done one or two months after the completion of adequate irradiation. This operation should never be attempted if tumor tissue stretches continuously from the breast up to and into the axilla.

The radium element pack may be substituted for high voltage roentgen rays if the process appears to be sharply defined, and we expect a more pronounced regression following its use than when high voltage roentgen rays are employed.

A continuous follow-up in this group is even more essential than in women of older age periods.

## SUMMARY

Cancer of the breast in young women is a much more menacing disease than it is in midlife or in old age. The course is often dramatic in its rapidity, almost simulating an infectious process. When the first symptom is a diffuse enlargement of the breast, a redness overlying the mammary gland or pain, surgical intervention is futile. A more careful examination of younger as compared to older women must be exercised before radical operation is undertaken. Early recurrence is

more frequent in younger than in older women, and indicates either a poorly chosen case for surgical intervention or poor surgical technic or both. In many of these patients, reliance must be placed entirely on radiation therapy. In well chosen cases, well planned adequate irradiation combined with a carefully performed radical amputation yields the best results.

# ESOPHAGEAL FISTULA IN THE EXPERIMENTAL ANIMAL *

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It has never been entirely clear that a failure of saliva to reach the stomach, owing to complete stenosis or to fistula of the esophagus, is of itself incompatible with normal growth, although such a possibility has been suggested by more than one author. Chevalier Jackson [1] noted the clinical benefit to patients with esophageal stenosis of their adding saliva to their food by preliminary chewing. In a personal communication Prof. A. J. Carlson mentioned a child with complete obstruction of the esophagus who was undoubtedly helped by a regimen of mastication of food before its introduction into the gastrostomy tube by which she was fed. Carlson ascribed the rapid gain in weight which he observed mainly to the secretion of gastric juice accompanying appetite and the chewing reflex, and questioned the importance of the actual presence of saliva in the food. Likewise, Prof. A. C. Ivy wrote us that he produced complete esophageal fistulas in dogs and maintained them for over a year by careful gastrostomy feeding accompanied by sham drinking. It seems probable, as Ivy suggested, that the benefit from mastication of food may lie, not in the saliva, but in a "cephalic conditioning of the digestive organs for both the motor and secretory work they are about to perform."

It is, of course, possible that continuous loss of salivary secretions from the body may cause a depletion of such mineral substances as sodium, calcium, potassium, chloride, phosphate, etc., contained in the saliva. Gamble and Ross [2] showed that pyloric obstruction may reduce the total chlorides of the body by one-third, with fatal results. The experiments of certain other workers suggested that a possibly analogous effect may be produced by obstruction higher in the intestinal tract than the pylorus—that is to say, at the cardia or even in the midesophagus. Haden and Orr [3] produced esophageal obstruction in dogs with rapidly

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1. Jackson, Chevalier: Arch. Pediat. **40**:324, 1923.
2. Gamble, J. L., and Ross, S. G.: J. Clin. Investigation **1**:403, 1925.
3. Haden, R. L., and Orr, T. G.: J. Exper. Med. **38**:477, 1923.

fatal results, their chemical studies showing a decrease in the chlorides of the plasma and an increase in nonprotein nitrogen. The explanation offered by these authors presupposed the rapid formation in the obstructed esophagus of a toxin which induced a fatal toxemia. With this hypothesis Wangensteen and Chunn [4] disagreed. They, too, reported a rapid lethal outcome following the operation, but felt that the administration of saline solution subcutaneously prolonged life by replacing salt and water that had been lost. The authors reached this conclusion from the fact that they had observed a decrease in the chlorides of the plasma and from noting the urinary excretion of salt and water. They stated that "on the same basis of loss of fluid and fixed base from the body, some alteration in the permeability of tissue is necessary to explain the death of an animal with esophageal obstruction, or a rabbit with duodenal obstruction that does not vomit." Later, the force of this argument was weakened when Gamble and McIver [5] explained the apparently anomalous behavior of the rabbit by showing that following pyloric obstruction chlorides accumulate in the stomach of this animal to such an extent that the body as a whole is depleted fully as much as though the gastric secretions had been vomited. In a recent paper White and Fender [6] showed that the retained secretions above a jejunal obstruction, when removed and reinjected below the obstruction, prolong life as efficiently as does saline solution, with no signs of toxicity.

Further work of an experimental nature by Andrus and Donnelly [7] recently appeared. These authors reported the death of animals with complete esophageal obstruction in an average of fifty-three hours; similarly, animals with complete esophageal fistula died in an average of seventy-three hours. In their experiments the administration of solutions containing sodium chloride or sodium chloride plus sodium bicarbonate appeared valueless. These authors stated that the cause of death is not clear and intimated that the loss of saliva may play an important rôle in the lethal outcome. Although this may be considered as a possibility, it is difficult to imagine a chemical mechanism to explain it, whereas loss of chlorides from the stomach in pyloric obstruction has a perfectly obvious physiologic implication.

4. Wagensteen, O. H., and Chunn, S. S.: Studies in Intestinal Obstruction: III. Simple Obstruction; a Study of the Cause of Death in Mechanical Obstruction of the Upper Part of the Intestine, Arch. Surg. **16**:1242 (June) 1928.

5. Gamble, J. L., and McIver, A.: J. Clin. Investigation **1**:531, 1925.

6. White, J. C., and Fender, F. A.: The Cause of Death in Uncomplicated High Intestinal Obstruction: Experimental Evidence to Show that Death Is Due Not to Toxemia, But to Loss of Digestive Fluids and Salts, Arch. Surg. **20**:897 (June) 1930.

7. Andrus, W. de W., and Donnelly, J. I.: Effects of Certain Operations on the Esophagus of the Dog, Including Esophageal Obstruction and Complete Esophageal Fistula, Arch. Surg. **20**:1 (Jan.) 1930.

Indeed, if the deaths observed could be explained by the loss of chemical substances from the body, pyloric obstruction should be more rapidly fatal than esophageal obstruction instead of less so, since saliva is lost in both instances and the gastric secretion is lost only in the former.

The feeling is now general that no satisfactory explanation for the rapid deaths observed in experimental esophageal obstruction or in fistula has been advanced. It is possible, as Ivy suggested, that neither toxemia nor loss of saliva is responsible, but rather some kind of obscure "reflex or pulmonary disturbance." It is possible that technical difficulties in producing low esophageal obstruction and fistula may play a part in the high mortality previously reported.

Whether or not one regards the rapid loss of salivary secretions as serious, there is evidence that the mere lack of saliva is not particularly harmful. In the first place, there are reports of at least two cases of congenital absence of all the salivary glands; one, cited by Blackmar,[8] occurred in a boy, 11 years old, and another, cited by Ramsey,[9] in a girl, aged 5, whose father was similarly afflicted. On the experimental side, Hemmeter [10] concluded from his work that extirpation of the salivary glands in dogs reduces gastric secretion, whereas Swanson [11] in repeating the work failed to agree with this observation.

There are apparently no data as to the degree of retardation in growth of the young animal that may be expected either from lack or from loss of saliva. Although this is a slightly different aspect of the problem from that discussed in the preceding paragraphs, it has been of chief interest to us because of its bearing on a case occurring in a 10 year old patient of Dr. Chevalier Jackson's, which it has been our privilege to study. This case, one of complete stenosis of the esophagus of eight years' duration, reported by us elsewhere, need be mentioned only in passing. So extreme was the child's malnutrition when we first saw her that we were almost willing to concede that her daily loss of saliva was perhaps largely to blame for her condition. Somewhat to our surprise, we found that as soon as we adapted the quality, consistency and caloric value of the patient's diet to the requirements of gastrostomy feeding, a remarkable change occurred. The weight increased from 37 to 65 pounds (16.8 to 29.5 Kg.) in ten months. During the last three months of that period the child was not permitted to mix any saliva with her food, a change that caused no slacking in her rapid rate of growth (a steady 3 pounds [1.4 Kg.] per month). More-

8. Blackmar, F. B.: Am. J. Ophth. **8**:139, 1925.

9. Ramsey, W. R.: A Case of Hereditary Congenital Absence of the Salivary Glands, Am. J. Dis. Child. **28**:440 (Oct.) 1924.

10. Hemmeter, J. C.: Science **26**:473, 1907; Tr. Am. Gastro-Enterol. A., **11**:5, 1908.

11. Swanson, A. M.: Am. J. Physiol. **43**:205, 1917.

over, there was no anemia, and roentgenologic examination of the bones showed normal structure. Our tentative conclusion was that in this instance the loss of saliva had not been intimately associated with the retarded growth and development.

## EXPERIMENTS

Since similar cases in man are rare, we decided to attempt to duplicate the condition in a litter of month old pigs, these being in some ways more suitable for comparison than are the more common laboratory animals. A three-stage operation was performed by Dr. I. S. Ravdin in the following manner:

With the animal under sodium amytal anesthesia, a 3 inch (7.6 cm.) incision was made just behind the posterior border of the lower end of the sternocleidomastoid muscle. The esophagus was freed for about 3 inches (7.6 cm.) and brought to the surface. Next, the midportion of the original wound was closed, leaving a portion of the esophagus external to the skin. Petrolatum and a gauze dressing were applied, and after a few hours the pig was allowed to drink small amounts of fluid. There was evidently some difficulty in swallowing, since the animals operated on voluntarily limited their intake of food to a fraction of what it had been previously. In from one to four days following the operation, an opening was made in the esophagus with a cautery, and liquid food was introduced into the stomach at regular intervals. Later the esophagus was divided, and we then had two esophageal fistulas: from the upper one saliva flowed, and into the lower one food and water were introduced.

Control animals were fed the same diet per kilogram of body weight as the animals operated on received by tube three times a day. The food was liquid, with milk as a basis, to which were added dextrose syrup, cod liver oil, tomato juice and vitavose to supply calories and vitamins.

Two groups of animals were used. The first group consisted of nine pigs, of which one, born late in December, was operated on on January 23. Of the remaining eight, born in one litter on January 4, six were subjected to operation (four on February 3 and two on March 5). In no instance did we have a sudden death following operation, the shortest period of survival being five days in a pig that had had diarrhea. A second pig died of mediastinitis nine days after operation, a third of abscess of the lung and pericarditis in fourteen days, and a fourth in twenty-six days of porcine scabies, which also killed one of the controls (not operated on) ten days later.

Four animals then remained, and of these one died on the hundredth day of a ruptured stomach, produced, we supposed, by the tip of the tube used for feeding. The other two animals operated on were killed on the hundred and thirty-second day when they had become too large for convenient handling.

Figure 1 illustrates the excellent gains in weight made by the three last mentioned animals despite their esophageal fistulas. To be sure, an even better gain was made by the control, but this is not surprising in view of the handicaps the animals operated on were under because of the abnormal method of feeding and the loss of fluid as saliva through the upper fistula. We experienced, indeed, considerable difficulty with

the feeding by tube, owing to a tendency on the part of the animals to regurgitate some of the food. Moreover, unless food was given very slowly, there were symptoms of painful distention of the stomach, due perhaps to absence of reflex relaxation. Undoubtedly, the psychic disadvantages of feeding by tube militated against the complete success of this procedure in the animals operated on.

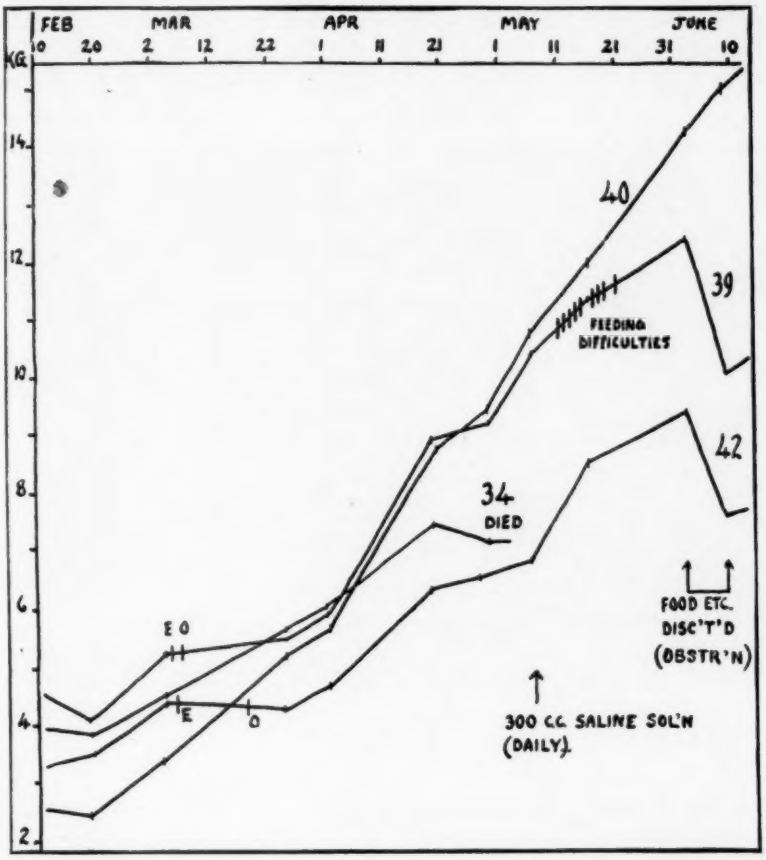


Fig. 1.—Weight curves of three pigs with experimental esophageal fistula and of one control (no. 40). Pig 34 was operated on on Jan. 23, 1930, and pigs 39 and 42 on the dates indicated by *E*, following which the esophagus was opened on the dates indicated by *O*. The esophagus was completely divided within seventy-two hours from the time it was opened.

Loss of saliva from the fistulas might have affected the pigs operated on unfavorably in two ways: (1) by depriving them of whatever digestive value this secretion may possess, and (2) by depleting the body of fluids and certain mineral ions. An estimate of the loss sustained is difficult to make, but in view of the fact that the salivary secretion in

man is reputed to be from 1,000 to 3,000 cc. daily, it is probable that the pigs lost from 200 to 500 cc. Certainly there was marked drainage from the salivary fistulas, a fact appreciated by the control animal, which developed the habit of sucking at the necks of his companions. It was to compensate for the salivary loss that we commenced giving a daily ration (300 cc.) of 8.9 per cent saline solution to the pigs when they were 3 months old (fig. 1). Apparently this did not exert a noticeable effect on the weight curves during the ensuing two months.

Shortly before we were ready to terminate the experiment we caused complete obstruction of the esophagus of the two pigs operated

Fig. 2.—Three pigs of the first litter: to the left, pig 40 (control); at the center, pig 42 (fistula), and at the right, pig 39 (fistula).

on that remained. This was maintained for ninety-six hours, the animals receiving no food or water. The obstruction was then removed, but food and water were withheld for another twenty-four hours. The animals were then fed as usual, and in three weeks one had gained over 1.5 Kg. Both were in excellent condition, but the second pig did not gain much weight, owing to increased regurgitation of food. Our conclusion was that the four days of acute obstruction had caused little disturbance aside from that of temporary starvation and dehydration.

A second litter (five pigs born on May 1, 1930) was obtained on May 28, and two of them were subjected to operation on June 6. Our object was to duplicate the previous experiment with a single modification, the addition of saline solution, from the beginning, to the

diet of the animals operated on. The only other differences were that the second litter was somewhat heavier than the first and benefited also from the improvement in our technic resulting from our experience in the postoperative management of the first litter.

The results were similar to those previously obtained, except that neither of the animals operated on and none of the controls died. The gain in weight following operation was more immediate and there were not the difficulties in feeding encountered in the previous experiment. The table lists the changes in weight.

The animals were slaughtered thirty-eight days after operation, as we felt that there was no object in carrying the experiment any further. It is worth mentioning, perhaps, that in the eighteen days between June

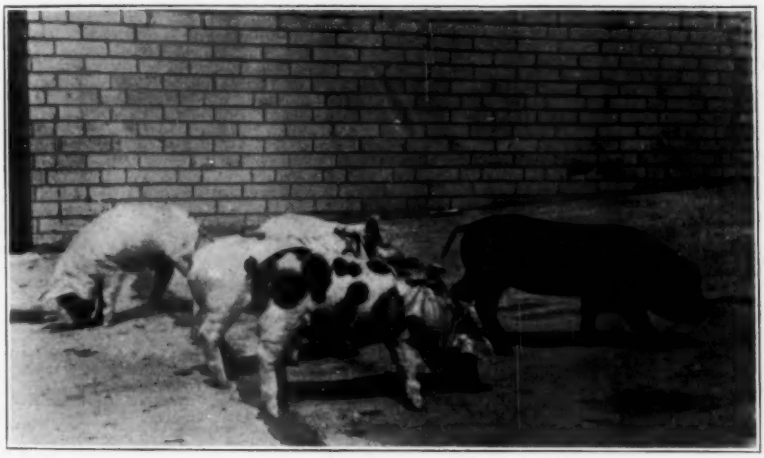

Fig. 3.—The second litter one week after the completion of the fistulas.

*Changes in Weight in Pigs Subjected to Experimental Esophageal Fistula*

| Date | Pig 66 Kg. | Pig 67 Kg. | Pig 68 Kg. | Pig 69 Kg. | Pig 70 Kg. |
|---|---|---|---|---|---|
| June 2 | 6.1 | 6.5 | 7.0 | 7.0 | 6.2 |
| June 6 | Control | Operated on | Operated on | Control | Control |
| June 7 | ... | Operated on | Operated on | | |
| June 9 | 6.9 | 5.9 | 7.0 | 7.4 | 7.0 |
| June 27 | 8.8 | 7.3 | 8.3 | 9.2 | 9.1 |
| July 14 | 9.4 | 8.2 | 8.5 | 10.0 | 10.3 |
| July 14 | | | (All animals slaughtered) | | |

9 and June 27 the animals operated on added 22 per cent to their weight and the controls 25 per cent, practically identical amounts. These figures may, however, favor the animals operated on to some extent, since part of the excellent gain in at least one animal may have been merely replacement of body fluids lost in connection with the operations of June 6 and 7.

## COMMENT

We attempted to investigate the effect of complete loss of saliva on the growth of a young animal (the pig). Somewhat to our surprise, our results appear to indicate that an esophageal fistula is not in itself particularly inimical to normal growth. The use of a three-stage operation probably contributed materially to the ease with which experimental fistulas were secured and maintained in our animals. We did not encounter instances of rapid death such as had been reported by various authors in the case of dogs. The explanation may hinge either on our use of a different animal or on our use of a different operation. So far as we have shown that loss of saliva is comparatively safe, we have perhaps helped to rule out that factor as an element in the lethal outcome of such operations on dogs. As to what other factors may be at work we have no data. Even in our animals there were periods of choking and cyanosis, which resulted either from aspiration or, as has been suggested by Ivy, from some type of reflex pulmonary disturbance. Possibly, in dogs this particular hazard is greater than in pigs. It would, perhaps, be interesting to attempt the three-stage procedure in dogs.

Chemical studies of the plasma would have been difficult to obtain. Moreover, we felt them to be superfluous in our experiments, as soon as it became apparent that the pigs did not die. In the rapidly growing young animal one would certainly not anticipate marked deviations from normal.

As to the clinical application of the work that we have outlined, we can suggest only that patients with esophageal obstruction or fistula require primarily individual dietetic care with particular attention to adequate calories in liquid form. The psychic benefit of preliminary mastication of food should not be overlooked as a measure of considerable secondary value.

## SUMMARY

1. In month old pigs, experimentally produced esophageal fistulas causing complete loss of saliva did not materially interfere with normal growth.

2. The operations were performed in three stages, without the complication of rapid death that had been reported in the case of dogs.

3. Apparently loss of saliva is less harmful, and proper dietary management more important, in these conditions than has been supposed.

# PARTIAL CHOLECYSTECTOMY *

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From the reports of the end-results of operations on the gallbladder, cholecystectomy has been shown to be the operation of choice in disease of the gallbladder with or without stones.

In patients with acute infections of the gallbladder, frequently bad risks, cholecystectomy is often technically difficult, and cholecystostomy is resorted to because of the ease and rapidity with which it may be executed, as well as the fact that drainage of the biliary tract may be indicated, and it affords a ready means of drainage of the biliary ducts. In from 25 to 50 per cent of the cases, this measure is only palliative, and cholecystectomy is later necessary because of persistent infection in the gallbladder with recurrent symptoms, the formation of stones or a biliary fistula. The ideal operation for even acute cholecystitis, provided it were safe, would be cholecystectomy or an operation that would destroy or remove the gallbladder, provide drainage of the bile passages and avoid the likelihood of a second operation. When, however, disease of the gallbladder is complicated by marked pancreatitis, diffuse cholangeitis or involvement of the common duct, the use of the gallbladder for drainage may outweigh the necessity for its extirpation, or it may be needed for a later cholecystenterostomy. Likewise, cholecystectomy is especially dangerous in the presence of jaundice, because of the likelihood of hemorrhage from the gallbladder fossa or liver, which may be difficult to control. Cholecystostomy may therefore be an operation of necessity or an operation of choice. In the cases in which cholecystostomy is used of neecssity, cholecystectomy would be preferable, but it is abandoned because (1) drainage is indicated, or (2) it is technically too difficult or impossible.

In 1923, in a case of multiple stones in the common duct and gallbladder with obstructive jaundice, I observed Dr. W. J. Mayo, instead of performing a cholecystectomy or the usual cholecystostomy, split the gallbladder from fundus to ampulla, remove the stones, and conclude by holding the gallbladder open its entire extent by properly placed drains.

A short time later, I was confronted by a case of gangrenous cholecystitis with stones in which complete cholecystectomy was definitely indicated; because of inflammatory induration about the cystic

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* Read in part at the Meeting of the Southern Surgical Society, Dec. 11, 1929.

duct, however, this method seemed technically inadvisable and probably dangerous. I therefore resorted to this same splitting of the gallbladder after removal of the stones, but supplemented it by trimming off the excess portion of the gallbladder close to the fossa in the liver, attempting to obtain the effect of a complete cholecystectomy, to permit drainage of the cystic duct and to avoid a two-stage operation, as is often necessary when only cholecystostomy is done. This partial cholecystectomy I have used in seven carefully selected cases. Convalescence has usually been uneventful; there have been no mortality and no evidence of peritonitis.

### OPERATIVE PROCEDURE

The gallbladder is exposed by an incision through the upper part of the rectus muscle. It is carefully surrounded by gauze packs, and the bile and fluid contents of the gallbladder are removed by aspiration. The fundus is then incised, and stones, if present, are removed. The gallbladder is dried and swabbed out with tincture of iodine. It is split from the fundus down to the cystic duct, and partially removed by trimming away the redundant part of each half down to the border of the liver. The bleeding from this cut edge is controlled by ligature or lock stitch up each side. Two or more cigaret drains are placed close about the cystic duct and brought out against the remnant of the gallbladder; the omentum is carefully tucked in between these drains and the duodenum, and the wound is closed.

### REPORT OF CASES

Brief abstracts of seven cases are appended to show, particularly, the end-results.

CASE 1.—*History.*—A man, single, aged 40, for six years had had a dull pain in the upper right quadrant of the abdomen, one-half hour after meals, which was relieved by soda. This pain recurred every month. There was no jaundice. Nineteen years before admission to the hospital, the patient had had a triple amputation, in which both thighs and the left arm had been removed.

*Examination.*—The patient had a round, thick, obese torso. There was no jaundice. The thighs had been amputated in the middle thirds, and good stumps had been left; the left arm had been amputated in the upper third. The abdomen was very fat, with slight tenderness over the right side of the hypochondrium. Roentgenograms showed a pathologic gallbladder. The results of the Fouchet test were positive.

*Operation.*—The abdominal wall was excessively thick and fat, the liver was high and enlarged, and the gallbladder was small, and thickened, with a tendency to obliterate and contained twelve stones. The common duct was normal on palpation. The gallbladder was exposed with great difficulty, and when removal was attempted, it ruptured near its base. The stones were removed, and a partial cholecystectomy was performed. The part of the gallbladder that was attached to the liver was allowed to remain, and three cigaret drains were inserted.

*Course.*—Vomiting continued until lavage on the second day. There was a brownish, serous discharge on the fifth day. The drains were removed on the eighth day. There was no biliary discharge. A small abscess (*Staphylococcus*

*aureus*) in the fat, lower angle of the wound appeared on the sixteenth day. The wound was completely healed, and the patient was discharged on the forty-second day.

Four years later, it was found that the patient occasionally belched gas. The wound was well healed, except for a postoperative hernia at the site of drainage. One month before the writing of this paper the patient was admitted to the medical service with jaundice and symptoms of obstruction in the common duct, which were relieved by Lyon biliary drainage. Twelve months later, there had been no recurrence of symptoms.

Fig. 1.—Splitting the gallbladder after aspiration (small inset), removal of the stones and swabbing with tincture of iodine.

Case 2.—*History.*—A woman, aged 51, married, who had no children, underwent a bilateral oophorosalpingectomy at the age of 25. For seven weeks before admission to the hospital, she had frequent attacks of severe cramps in the upper right quadrant of the abdomen, radiating to the right shoulder and requiring morphia for relief. There was slight jaundice at the onset of the symptoms, with nausea and vomiting.

*Examination.*—The patient was obese and did not have jaundice. Marked tenderness, rigidity and an indefinite mass were present in the upper right quadrant of the abdomen. There was a well healed suprapubic scar. Examina-

tion of the blood revealed: white corpuscles, 17,200, and polymorphonuclears, 78 per cent. Urinalysis gave negative results.

*Operation.*—The patient was operated on one-half day after admission. The gallbladder was three times its normal size, gangrenous near its base and filled with stones (546) and thin, pale pus, not bile-stained. The gastrocolic omentum was adherent to it and was very thick and edematous. There were two large stones in the cystic duct, while examination of the common duct gave negative results. The gallbladder was isolated by packs, aspirated (the stones removed), swabbed with tincture of iodine and then split down through the ampulla. Partial cholecystectomy was done. Four cigaret drains were inserted. The culture from the gallbladder was sterile.

*Course.*—There was free biliary discharge for ten days, but the drains were removed on the seventh day. The patient was discharged on the twenty-first day, with the wound healed.

Four years later, the patient was found to be in excellent health, having had no indigestion, pain or discomfort since the operation.

CASE 3.—*History.*—A woman, aged 39, married, who had three children, had had pain in the epigastrium, radiating to the right shoulder and back by "spells" for three years. She had had the present attack for the last twelve days and intermittent cramps with vomiting, water brash and pain after the ingestion of food. Ten years before, she had had a complete hysterectomy.

*Examination.*—The patient was fat and not jaundiced. Marked tenderness, rigidity and an indefinite mass were present in the upper right quadrant of the abdomen. There was rigidity of the entire right rectus muscle, and a well healed suprapubic scar. Examination of the blood revealed: white corpuscles, 6,400; polymorphonuclears, 82.5 per cent; hemoglobin, 80 per cent, and red corpuscles, 4,300,000. Roentgenograms showed a pathologic gallbladder. The Wassermann reaction was negative.

*Operation.*—The patient was operated on four days after admission. The gallbladder was thickened, inflamed and filled with thin fluid pus but no bile. Firm adhesions bound the omentum to the gallbladder, and one stone was impacted in the cystic duct. Examination of the common duct gave negative results. The gallbladder was carefully isolated by gauze packs, split from the fundus to the cystic duct, the redundant portion excised, and the stone removed. A lock stitch was used to control the oozing from the cut surfaces. Four cigaret drains were placed in the gallbladder fossa. The omentum was carefully placed against the under surface of the liver. Culture from the gallbladder showed *B. mucosus-capsulatus.*

*Course.*—The patient was febrile, with a temperature ranging from 100 to 102 F. for two days. There was biliary drainage on the fourth day. The drains were removed on the sixth day, and replaced by a tube. Purulent biliary discharge followed, and the tube was removed on the fifteenth day. The patient was discharged on the twenty-third day, with the wound practically healed, except for a superficial sinus with no drainage.

There was no recurrence of pain or indigestion for four years; it has not been possible to trace the patient for the last two years.

CASE 4.—*History.*—A woman, aged 45, married, who had four children, for five months had had attacks of severe epigastric pain radiating to both shoulders and back, with vomiting. These attacks occurred two or three times a month. The last attack was on the day before admission.

*Examination.*—The patient was stout, with a faint icterus and marked tenderness in the upper right quadrant of the abdomen. Examination of the blood revealed: white corpuscles, 15,000; polymorphonuclears, 79 per cent, and an icterus index of 13. The roentgenogram showed gallstones and a poorly filling gallbladder.

*Operation.*—The patient was operated on three days after admission. The liver was cirrhotic with a huge gallbladder, the walls of which were 1 cm. thick. One large stone was impacted in the cystic duct. A hard, indurated omentum was

Fig. 2.—Suturing the cut margins of the gallbladder with lock stitch at the edge of the gallbladder fossa, the remainder of the gallbladder having been removed.

adherent to the gallbladder. Examination of the common duct gave negative results. The gallbladder was isolated, aspirated, incised and swabbed thoroughly with tincture of iodine. The stone in the cystic duct could not be removed until the gallbladder was split down to the cystic duct. The free portion of the gallbladder was cut away, and the cut edge sutured with a lock stitch. Four cigaret drains were used to hold the gallbladder fossa open and to drain the cystic duct, and the omentum was placed against them. A culture from the gallbladder was sterile.

*Course.*—The patient had a slight fever for four days, with only a serous bile-stained discharge. The drains were removed on the sixth day. She was discharged on the thirteenth day, with a slight, persistent sinus.

Two years later, the patient was completely relieved from symptoms, the wound had healed well, and there was no hernia. She had had no pain in the upper quadrant of the abdomen or indigestion since the operation. Recently, she had had a pain in the lower part of the right side suggesting appendicitis.

CASE 5.—*History.*—A woman, aged 45, married, who had no children, had had a hysterectomy for fibroids ten years before admission to the hospital. She had never been pregnant. She had had attacks similar to her present illness one and two years before, but these had been mild and of brief duration. Twenty-four hours before admission to the hospital, while she was washing clothes, she was seized by a sudden, severe pain, with vomiting, which steadily persisted, and which was relieved by morphine two hours before admission.

*Examination.*—The patient was moderately obese and slightly jaundiced; her teeth were in bad condition, and there were marked rigidity and tenderness in the upper right quadrant of the abdomen. No mass could be palpated, and there was a well healed suprapubic scar.

Examination of the blood revealed: white corpuscles, 26,650; polymorphonuclears, 94 per cent, and icterus index, 8. Urinalysis showed a trace of albumin, sugar and bile.

*Operation.*—The patient was operated on on the day after admission. There was an excess of turbid, peritoneal fluid. The gallbladder was very large and completely detached from the liver, except at the ampulla and cystic duct. There was no gallbladder mesentery. The gallbladder was thick and acutely inflamed, containing many large and small stones, with one impacted in the cystic duct. The common duct was edematous, but there was no stone. The pancreas was thickened. The gallbladder was isolated and aspirated, the stones were evacuated, and the entire cavity was swabbed with tincture of iodine. It was then resected, except for a small portion adherent to the liver above the cystic duct for 2 cm. This, and the cystic duct were split wide open, the excess margins trimmed away, and the cut surface sutured by lock stitch. Tincture of iodine was applied to the remnant that remained, and three cigaret drains were placed in and about the cystic duct. Streptococcus was cultivated from the bile of the gallbladder.

*Course.*—There was little if any drainage, with slight fever for five days and very light nausea. The drains were removed on the sixth day. The patient was discharged on the eleventh day, with a small discharging sinus.

Three months later the wound had healed well. There was a slight keloid. The patient was able to eat liberally without indigestion.

One year later, the patient was entirely well, with no recurrent pain or indigestion.

CASE 6.—*History.*—A man, aged 73, married, had had upper abdominal pain for many years, steadily increasing jaundice for two months, with slight variable abdominal pain, anorexia and normal stools.

*Examination.*—The skin was bronzed, and there was an icteric tint to the sclerae. The teeth were abscessed and there was upper dorsal kyphosis. Emphysema was also present. The liver was large with an irregular edge, and there was tenderness but no definite mass in the region of the gallbladder. Roentgenograms showed the duodenum to be deformed from pressure from without. The icterus index was 13.5. Examination of the blood revealed: white corpuscles, 12,850;

polymorphonuclears, 70 per cent; red corpuscles, 3,930,000, and hemoglobin, 80 per cent. There was a trace of albumin and hyaline casts in the urine.

*Operation.*—The patient was operated on three days after admission. There was marked cirrhosis of the liver. The gallbladder was hugely distended and almost gangrenous, containing 120 cc. of thin, pale green fluid and numerous small stones. The hepatic flexure was adherent to the fundus. There was induration of the cystic and common ducts. The entire pancreas was thickened. The adhesions were separated, and the gallbladder was isolated, aspirated, incised widely and swabbed with tincture of iodine, and the stones were removed. Two

Fig. 3.—*A*, drainage of the area of the gallbladder with cigaret drains. *B*, the omentum tucked between the drains and the nearby viscera.

stones were also taken from the cystic duct. Partial cholecystectomy was performed, but no opening into the common duct was found. One tube was placed in the cystic duct, and four cigaret drains were inserted. A culture from the gallbladder was negative.

*Course.*—There was no drainage from the cystic duct, but on the fourth day, the jaundice was much decreased. The drains were taken out on the sixth day. The patient was discharged on the twenty-first day, free from jaundice, with the wound well healed.

Six months later, the patient was completely relieved and well.

CASE 7.—*History.*—A woman, aged 73, married, had had previous attacks twelve years and one week before admission. Two days before, severe pain developed in the upper right quadrant of the abdomen, which radiated to the shoulder and which persisted fairly constantly. Morphia was given for relief. There was slight jaundice.

*Examination.*—There were tenderness, rigidity and a mass in the upper right quadrant of the abdomen. Urinalysis gave negative results. Examination of the blood revealed: white corpuscles, 16,900; polymorphonuclears, 80 per cent, and blood urea, 23.

*Operation.*—The patient was operated on four days after admission. Spinal anesthesia was used. The gallbladder was completely gangrenous, moderately enlarged and surrounded by thick, plastic omental adhesions, partially perforated near the fundus. It contained thick, pale pus and three large, and numerous small, stones. One large stone was impacted in the cystic duct. The common duct and pancreas were normal. A culture from the gallbladder grew *Bacillus coli.* The gallbladder was aspirated and split wide open, and the stones were removed. Partial cholecystectomy was performed, and one tube was placed in the stump of the cystic duct. Four cigaret drains were also inserted..

*Course.*—There was free biliary drainage on the fifth day, and all drains were removed on the ninth day. The patient had no fever, and was discharged on the eighteenth day with a wound completely healed, except for a small sinus.

Three months later the wound was well healed and there had been no hernia. The patient was well and free from pain and indigestion.

*Comment.*—It will be observed that partial cholecystectomy has been used six times in cases of acute cholecystitis with a stone impacted in the cystic duct, and once in the case of a hugely fat man with a thick, round torso, in which the operation was exceedingly difficult and complete cholecystectomy seemed impossible.

The patients with impacted stone in the cystic duct have shown no evidence of recurrence. Two have been followed for four years. The patient in case 1 recently had symptoms of involvement of the common duct.

Tincture of iodine was used to sterilize and destroy the mucosa of the remnant of the gallbladder. The actual cautery, however, may be more effectual, as Pribram [1] recently suggested.

## COMMENT

Partial cholecystectomy, I find, is not a new procedure. In 1899 and again in 1900, W. J. Mayo [2] reported cases, particularly of obstruction of the cystic duct, in which removal of the stones and the mucous membrane of the gallbladder was done instead of complete cholecystectomy. Partial cholecystectomy was described in 1920 by Ben-

1. Pribram, B. O.: Zentralbl. f. Chir. **55**:773, 1928.

2. Mayo, W. J., in Mayo, W. J., and Mayo, C. H.: Collection of Papers Previous to 1909, vol. 1, pp. 348 and 355.

golea.[3] In 1921, E. D. Martin[4] cited five cases of acute cholecystitis in which he had removed the stones, split the gallbladder and held it wide open with drains.

In 1923, De Martel,[5] in a series of fifty-two operations on the gallbladder reported that in two, in which it was difficult to separate the ampulla and the cystic duct from adjacent structures, he split the gallbladder from fundus to ampulla, divided the cystic duct and cut away the free part of the gallbladder, swabbed the remaining portion with tincture of iodine and drained it. Both patients recovered.

In 1924, Zabala and Bengolea[6] cited four cases of partial cholecystectomy with recovery; in one there was a mass of adhesions about the gallbladder; in another a calculus was impacted in the cystic duct, which was firmly indurated and adherent to the common duct; and in a third, a piece of the gallbladder was left near the cystic duct because of the friability of the tissue. They expressed the belief that the operation is indicated in severe suppurative cases in which resection would be fatal. The gallbladder is split and the stones are removed. Then the gallbladder is resected, leaving a portion attached to the liver; the mucosa of this remnant is curetted, and tincture of iodine is applied.

Pauchet[7] decided that partial cholecystectomy was indicated: (1) in feeble or icteric patients, with stones in the common duct and gallbladder; (2) in atrophic gallbladder with stones; (3) in cases of subacute or acutely inflamed gallbladder adherent to the adjacent organs, and in (4) suppurating cholecystitis with fever. He believed that this operation avoids cholecystectomy when cholecystectomy would give a mortality of 50 per cent. He followed Zabala and Bengolea's technic, except that the remaining mucosa is swabbed with ether as well as with tincture of iodine, and when there are strong adhesions to the nearby intestines, the gallbladder is freed from the liver, and the portion adherent to the intestine is allowed to remain. The operation has been performed only in carefully selected cases in which cholecystectomy seemed to be indicated, but would be a dangerous procedure because of technical difficulties or the amount of infection present. In 1927, Gatch[8] and Zimmerman[9] referred to similar procedures before the Western Surgical Association.

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3. Bengolea, A. J.: Bol. y trab. de la Soc. de cir. de Buenos Aires, Nov. 26, 1920, p. 285.
4. Martin, E. D.: New Orleans M. & S. J. **74**:204, 1921.
5. de Martel: Bull. Soc. de Chir. **49**:306, 1923.
6. Zabala, A., and Bengolea, A. J.: Lyon chir. **21**:281, 1924.
7. Pauchet, V.: Gaz. de hôp. **97**:1077, 1924.
8. Gatch, W. D.: Tr. West. Surg. Assn., 1927, p. 345.
9. Zimmerman: Tr. West. Surg. Assn., 1927, p. 341.

## CONCLUSION

Partial cholecystectomy has, and should have, a restricted field. In patients in whom the surgical risk is thought to be great it should not replace cholecystostomy. Evidence of recurrent disease in the biliary tract has appeared in but one of seven cases, and in none of the cases in which a stone was impacted in the cystic duct. If argument were justified, based on so few cases, it would seem that this operation tends to act as a cholecystectomy—it prevents reformation or regeneration of the gallbladder and yet permits drainage as in cholecystostomy. It might, therefore, also have a field of usefulness in the rare type of secondary operation on the gallbladder in which, owing to adhesions or to a liver that cannot be rotated, cholecystectomy, although indicated, would be impossible.

## SUMMARY

1. Partial cholecystectomy in properly selected cases seems a safe procedure.

2. Its chief indication is in acute cholecystitis when a cholecystectomy is indicated and is technically impossible or unsafe, particularly in cases of an impacted stone in the cystic duct.

3. It should never be used when cholecystectomy can be safely performed.

4. The end-results in seven cases are reported.

# SPONTANEOUS RUPTURE OF THE URINARY BLADDER

## REPORT OF TWO CASES *

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Rupture of the bladder by penetrating wounds was familiar to the ancients. Homer describes the death of Phereclus due to a spear wound passing from the buttock, through the perineum into the bladder. Spontaneous rupture, however, seems to have been recognized rather late in the history of medicine, as the first recorded case that an extensive review of the literature reveals is that of Pierus in 1279. For the next five centuries the cases of rupture of the bladder that were found were all of the traumatic type. The next reported case of spontaneous rupture was presented by Johnstone in 1773. Reports have become increasingly frequent since that time, until it is possible to review forty such cases to date. To these are added the two cases reported in this article.

The paucity of cases may seem surprising, but it is partially due to the definition of the term "spontaneous rupture." The various interpretations of its meaning by different authors has led to considerable ambiguity in the classification of cases. Some authors, for example, have reported as "traumatic" cases in which a fall or a blow caused the rupture of the distended viscus without any penetrating wound of the bladder, while other writers have considered similar cases spontaneous. For this type of case, the term "concussional" is proposed. Again, fistulas between the bladder and the intestinal tract due to inflammatory adhesions between the two structures with destruction of tissue at the point of contact have been considered under the heading of rupture of the bladder by some authorities and as essentially enterologic lesions by others. They should be placed in the same category as vesicovaginal and vesico-uterine fistulas, and not be classified under ruptures.

A clearer classification will be achieved if the term "rupture" is used to connote an evacuation of the bladder contents into a closed cavity, of which only two are accessible, namely, the perivesical space and the abdominal cavity. The term spontaneous rupture should be applied to those cases resulting from pathologic changes in the wall of the bladder or obstructive lesions at the neck of the bladder or in the urethra,

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* From the Gynecological Service of the Rhode Island Hospital.

irrespective of the presence or absence of pathologic changes in the bladder. With this redefinition in mind, the following classification is proposed for cases of rupture of the bladder:

I. Traumatic
  A. Penetrating Wounds
    1. By objects entering from outside the body
    2. By objects entering from inside the body as
      (*a*) Bone fragments
      (*b*) Foreign bodies harbored within the body
  B. Concussional (Falls or Blows Not Causing Penetrating Wounds of the Bladder)

II. Spontaneous
  A. Inflammatory Lesions of the Wall of the Bladder
    1. Intramural origin
    2. Extramural origin
  B. Malignant Disease of the Wall of the Bladder
    1. Intervesical
    2. Intravesical
    3. Extravesical
  C. Obstructive Changes at the Neck of the Bladder
    1. Prostatic enlargement
      (*a*) Benign
      (*b*) Malignant
      (*c*) Inflammatory (including seminal vesiculitis)
    2. Calculi
    3. Paralytic
    4. Uterine and adnexal disease in the female
    5. Occurring during labor
  D. Obstructive Lesions in the Urethra
    1. Strictures
    2. Valves diverticula
    3. Tumors
    4. Calculi
    5. Peri-urethral inflammation
    6. Peri-urethral tumors

## REPORT OF CASES

CASE 1.—R. S., a girl, aged 9½ years, was admitted to the orthopedic service on Nov. 22, 1928, complaining of a limp. The father and mother were living and well; there were six siblings living and well; none was dead. There was no tuberculosis in the family. The child had been admitted to the hospital on Sept. 21, 1922, with an infected right foot. She was discharged in ten days, against advice, with the foot and lower part of the leg swollen and reddened and a temperature of 100 F. She was readmitted on May 18, 1924, with osteomyelitis (nontuberculous) of the right os calcis, right hip and right ulna. She was again admitted on Sept. 11, 1924, with abscess in the right heel from osteomyelitis of the os calcis. On July 2, 1926, she came to the hospital for operative correction of the deformity of the right hip. She had been well until one week before the last admission, when she began to limp, developed pain in the right hip and fever.

*Examination.*—On physical examination, areas of dulness were found on percussion at the apex of both lungs, with moist râles on both sides throughout. The fremitus was normal. The edges of the kidney, liver and spleen were not palpable. There was tenderness in the right lower quadrant extending down into the right groin and most marked over the hip joint. No masses, spasm or rigidity were noted. Motions of the hip were limited in all directions and were painful. Roentgen examination on Nov. 23, 1928, showed no evidence of pathologic process in the dorsal or lumbar spine. There was considerable increased density in the lung markings. The changes noted in the chest could be due to tuberculosis. On the day of admission, the urine was clear, yellow, acid, with a specific gravity of 1.026 and no albumin or sugar; the sediment showed a rare leukocyte. On November 23, the leukocyte count was 15,000, with 83 per cent polymorphonuclears. The vaginal smear was negative.

On December 7, frequency, burning, spasm and extreme dysuria suddenly developed. The urine passed was thick with pus. The child had never before had any urinary symptoms. Urinalysis showed thick yellow urine with a specific gravity of 1.024, acid, no sugar, a large trace of albumin and sediment loaded with pus. No tubercle bacilli were seen.

*Operation and Course.*—On December 12, an incision was made, and the abscess in the right hip was drained. There was a fluctuant area over the old scar. A considerable quantity of watery, blood-colored fluid flowed from the wound. A cigaret drain was inserted, and a catheter was introduced into the bladder, but no urine was obtained. On pressing the lower part of the abdomen, a mucopurulent fluid was expressed from the vagina. Rectal examination gave negative results, no areas of fluctuation or induration being noted (Dr. Murray Danforth). On December 12, a culture of the pus from the hip showed gram-positive cocci, *Staphylococcus aureus.* No tubercle bacilli were found in the smears. The child had voided nothing by the urethra since operation, but on December 22, the dressing on the wound in the right hip was saturated with urine. Cystoscopy (Dr. Stone) was done with the child under gas-oxygen anesthesia. A no. 18 F. cystoscope entered the bladder easily. Thick pus was obtained. The fundal mucous membrane was everywhere intensely red and swollen. No stones, ulcers, tumors, diverticula or trabeculae were seen. The trigone, which could not be defined as to its limits, as well as the sphincter partook of the generalized inflammatory reaction. The right orifice was vulva-like and about 1 cm. in length. It admitted a no. 5 x-ray catheter, which passed freely to the pelvis. The left orifice was normal and admitted a catheter to the pelvis. About 2 cm. directly posterior to the right orifice was a circular opening in the wall of the bladder which looked like the mouth of a diverticulum; a catheter was passed into this up to 10 cm., giving the impression that it coiled up out of sight as it was fed into the orifice.

The urine from the kidneys was slightly blood stained, and the flow was rapid and regular. Culture of the urine from both kidneys was sterile. A smear of the urine from the right kidney showed few white blood cells, few epithelial cells and a moderate number of red blood cells; that from the left kidney showed few red blood cells, few white blood cells and epithelial cells. Phenolphthalein, injected intravenously, appeared in the urine from the right kidney in eight minutes and in that from the left kidney in twelve minutes. In fifteen minutes, the urine from the right kidney showed 2.5 per cent phenolphthalein and that from the left kidney 4 per cent. The stain for tuberculosis was negative; the guinea-pig test

was also negative. The capacity of the pelvis of the right kidney was not obtained, but into the left kidney 5 cc. of 12.5 per cent solution of potassium iodide was injected.

Twenty-five cubic centimeters of potassium iodide was injected through the catheter, introduced into the rent in the wall of the bladder. The pelvis of the left kidney and the calices were well outlined after injection. There were many dense, irregular shadows at the level of the third and fourth lumbar vertebrae, probably due to calcified glands. There was an opaque catheter in each ureter. There was also a third catheter projecting to the right of the median line with

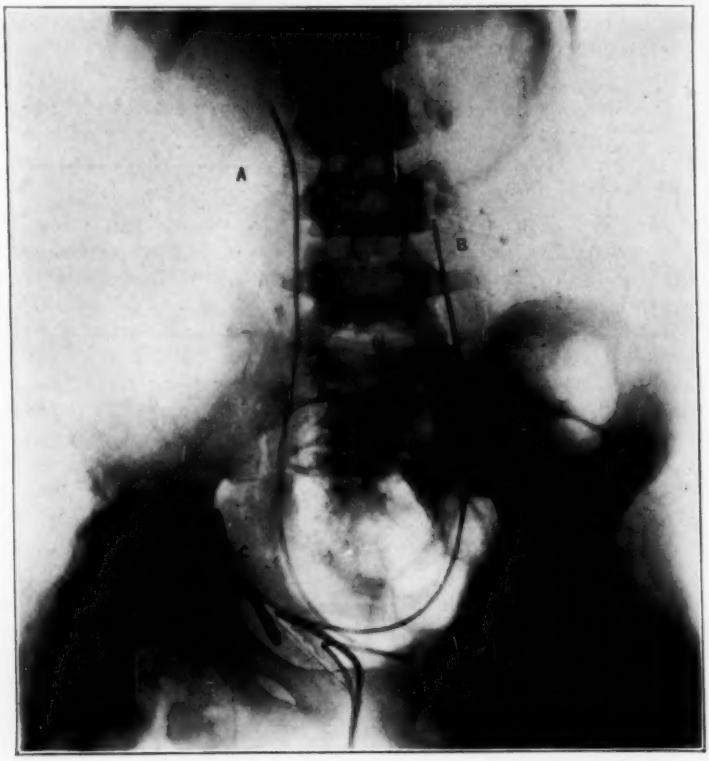


Fig. 1 (case 1).—Catheter in position; *A*, catheter in the right ureter; *B*, in the left ureter and *C*, in the perivesical tissue.

several loops, apparently outside the wall of the bladder. The loops were probably in the tissues outside the ruptured area. The opaque solution had been injected through this catheter and could be seen near the pelvic brim and also overlying the wing of the right ilium (Dr. James Boyd) (figs. 1 and 2).

On Jan. 7, 1929, after the injection of sodium iodide into the bladder, a cystogram of the region of the bladder and right hip showed evidence of the opaque material extending from the bladder laterally, then downward anterior to the acetabulum, then downward and posterior to the femur to the lateral aspect of the thigh (Dr. Philip Batchelder) (fig. 3). Although the patient had voided

nothing by the urethra from December 7 to 23, she urinated within six hours of the cystoscopic examination and has continued to do so. Micturition was associated with considerable dysuria for about two weeks. The urine was loaded with pus cells for about three weeks. Microscopic examination of the sediment after centrifugation showed a few leukocytes on February 15, and only a rare leukocyte on April 10. The sinus at the right hip became permanently closed on January 31. Medicinal measures alone were used, compound methylene blue (methylthionine chloride, U.S.P.) being the only urinary antiseptic presented. Convales-

Fig. 2 (case 1).—After the injection of potassium iodide solution into the left kidney pelvis and sinus. *A* shows the catheter in the right ureter; *B*, the pyelogram of the pelvis of the left kidney; *C*, potassium iodide solution in the bladder; *D*, in the perivesical space; *E*, passing anterior to the anterior superior spine; *F*, around the acetabulum and head of the right femur.

cence was complicated by an acute inflammation of the middle ear on January 23, which soon subsided. The temperature remained normal after February 21, and on April 12, the patient was discharged to the Crawford Allen Memorial Convalescent Home.

Case 2.—*History.*—R. W., a man, aged 67, was admitted to the Rhode Island Hospital on Nov. 25, 1891, dangerously ill, complaining of pain in the left lower quadrant of six days' duration. He had had frequency and nocturia for some years and for one year had been troubled by "gravel" passing by the urethra. Since the onset of the present illness, he had passed only a few drops of thick, bloody urine. The temperature was 104 F. on admission, and the patient was toxic and difficult to arouse.

*Examination.*—Physical examination showed as noteworthy features marked tenderness and spasm and some induration in the left lower quadrant. There

Fig. 3 (case 1).—Cystogram. *A* shows the catheter in the ureter; *B*, the potassium iodide solution in the bladder; *C*, in the perivesical space; *D*, potassium iodide solution near the acetabulum; *E*, back of the great trochanter and passing posteriorly to a subcuticular position, *F*.

was a right inguinal hernia, which had been present for twelve years. A catheter was passed into the bladder with ease, but only a few drops of blood-stained purulent fluid was obtained. Boric solution, 550 cc., was introduced through the catheter, but only 30 cc. was recovered. By sound, an endeavor was made to find a possible vesical calculus but none was demonstrated.

*Operation and Course.*—Operation was performed on November 27 by Dr. Mitchell. A suprapubic midline incision was made and the peritoneum opened,

but no fluid was found in the abdominal cavity. The peritoneum was repaired, and the incision carried down over the bladder, which was opened in the midline. No stones or urine were found, and no rupture was located. There was extensive extravasation of urine throughout the left side of the space of Retzius, and amid much necrotic and purulent matter a vesical calculus the size of a bean was found. The bladder was closed around a drainage tube, and a drain was placed in the area of extravasation. The wound was then closed in layers about the two drains. The patient left the operating room in a state of shock. He did not rally from the operation; no urine was discharged while in the hospital, and he died on November 29.

Case 1 has four points of interest: 1. It demonstrates the distance from which inflammatory lesions may burrow to reach the wall of the bladder and then cause enough inflammatory reaction to result in rupture. 2. What part the trigone and sphincter played in producing the rupture is not clear. Obviously there was a profound disturbance of the sphincteric function if the failure to void was due to the pathologic process at this point. There are two possibilities. The early frequency and dysuria may have expressed an irritation from perivesical inflammation, which, as it progressed, rendered the trigonal muscle incapable of action, and the subsequent retention precipitated the rupture, or the rupture may have occurred early, and the free drainage of urine through the rent made voiding unnecessary. 3. It is also obvious that some factor involved in the cystoscopic examination so altered conditions that the patient voided within six hours of the procedure, although for the ten preceding days she had passed nothing through the urethra. The factors involved were mechanical dilatation of the neck of the bladder, prolonged and thorough irrigation of the bladder and sinus tract with boric solution and injection of 12.5 per cent potassium iodide solution into the site of the rupture. 4. The fourth point of interest is spontaneous cure in a case of spontaneous rupture of the bladder. The second case reported here is interesting more as a curiosity than for its scientific value. It occurred before the modern era of careful study and case recording, and the hospital record was far from complete. Apparently a vesical calculus caused sufficient inflammatory reaction in the wall of the bladder to penetrate it and emerge in the perivesical tissues. Two other possibilities present themselves. The calculus may have become impacted in the neck of the bladder and caused a rupture by obstruction and later may have fallen out of the bladder through the rent, although in such a case one would have expected the rent to be posteriorly at the vault, which would have caused an intraperitoneal rupture; or there may have been a rupture of the ureter proximal to the physiologic intramural constriction, as no rent in the bladder was discovered. But in such a case the greatest changes would have been expected at the base, rather than laterally and anteriorly.

## INCIDENCE

At the Rhode Island Hospital, 1868-1929, 2 cases of spontaneous rupture were found in 226,632 total medical and surgical admissions. Quick reported the incidence of all types of ruptures of the bladder as follows: Cook County Hospital, 1889-1893, 5 cases of all types in 8,000 surgical admissions; St. Bartholomew's Hospital, 1869-1875, 2 traumatic cases in 16,711 admissions, and Episcopal Hospital, Philadelphia, 1900-1905, 3 intraperitoneal cases in 8,367 admissions.

## PATHOLOGY

In all cases either one of two conditions was present at the time of the rupture; in only a few were both present simultaneously. There was either chronic or temporary obstruction to the urinary outflow, or there was a destructive lesion of the wall of the bladder. There were twenty-one cases of obstruction, and only twelve of lesions of the bladder, while in nine the description was not sufficient to determine the type (table 1). In eighteen of the cases, no abnormality of the wall of the bladder was discovered at the site of the rupture. In thirty of the cases of intraperitoneal rupture, the site is recorded. In twelve cases, rupture occurred at the vault in the midline or just below it, which is as would be expected in that developmentally this is one of the weak points in the musculature of the bladder, and structurally it is the part furthest removed from the support of surrounding tissues. In the only case reported in which rupture occurred near the base of the bladder, an old scar from a retroperitoneal hematoma was found at the site. Again, as would be expected, the preponderance of intraperitoneal ruptures resulted from an obstructive pathologic process (fifteen intraperitoneal to six extraperitoneal); whereas the preponderance of extraperitoneal ruptures occurred in the same ratio, in cases in which there was a pathologic process of the vesical wall.

There were two cases of extraperitoneal rupture dependent on obstructive pathologic process which are interesting because of the site of the ruptures. One was just medial and posterior to the right ureteric orifice, while the other bore the same relation to the left orifice. These two points are apparently inherently weak, despite surrounding structures, as they are the most frequent site of diverticulae, especially of the congenital type.

As to the pathologic process in the wall of the bladder in the ten cases in which such a process was found, the predominant lesion was ulceration of the wall. In the cases in which the lesions were obstructive in twenty-four the descriptions were clear, urethral stricture occurred nine times, dry labor five and prostatic hypertrophy three times (table 1).

## ETIOLOGY

The precipitating cause, over and above the situation created by the pathologic process present, in twenty-one cases in which a description was given in the case reports, was invariably a sudden increase in intra-abdominal pressure. The specific causes are as follows: manual expression of the placenta five days post partum, 1; rupture of distended bladder during labor, 5; attempted micturition during acute retention, 6; intoxication (no history or evidence of any type of trauma), 3; straining at the stool, 3; sudden lifting of a weight, 3.

## MORTALITY

The mortality in rupture of the bladder before 1900 was appalling. The elder Lally, in 1817, was the first person to maintain that a patient

TABLE 1.—*Pathology and Site*

| Pathology | Number | Site | Number |
|---|---|---|---|
| Bladder | | Intraperitoneal type | 30 |
| No lesion found | 21 | Top of vault in midline | 6 |
| Ulcer | 4 | Just below top in midline | 6 |
| Cancer | 2 | Posterior inferior fundus | 2 |
| Diverticulum | 1 | Right side near vault | 1 |
| Trabeculum | 1 | Left side near vault | 1 |
| Old scar | 1 | Extraperitoneal type | 12 |
| Calculus | 1 | Middle of trigone | 1 |
| Prostatic hypertrophy | 3 | Anterior wall of fundus | 1 |
| Urethra | | Right near ureteric orifice | 1 |
| Stricture | 9 | Left near ureteric orifice | 1 |
| Calculus | 2 | Site in obstructive lesion | |
| Impervious | 1 | Extraperitoneal | 6 |
| Perivesical cellulitus | 2 | Intraperitoneal | 15 |
| Retroversion of uterus | 1 | Site in lesions of bladder wall | |
| Dry labor | 5 | Extraperitoneal | 15 |
| Paralysis | 1 | Intraperitoneal | 6 |

might recover from such an accident. S. S. Smith recorded seventy cases of all types up to 1851, with a mortality of 93.5 per cent. By 1893, A. R. Quick was able to show improvement as far as traumatic intraperitoneal rupture was concerned, presenting a mortality of 24.1 per cent. Since 1900, there has been a marked diminution of fatalities.

If only the cases of spontaneous rupture are considered (table 2), the ratio of improvement is much the same. Full descriptions of the treatment and of the end-results were available in only twenty-seven cases. The mortality in all cases of spontaneous rupture up to 1900 was 78.9 per cent, while that from 1900 to the present fell to 27.2 per cent. The rates for intraperitoneal spontaneous ruptures are uniformly higher than those in which the rent opened extraperitoneally. Among the former, the mortality rate was 92.3 per cent prior to 1900 and 45.4 per cent subsequently. The latter figure is reduced to 33.3 per cent if the two cases are excluded in which death occurred so promptly that treatment could not be instituted.

The extraperitoneal type of spontaneous rupture seems to be the least fatal. Even in the period up to 1900, the mortality rate was only 50 per cent as compared with 92.3 per cent for intraperitoneal rupture. In the last thirty years, there are no recorded fatalities in perivesicular extravasation, in sharp contrast to a mortality rate of 45.4 per cent for the intraperitoneal type.

## DIAGNOSIS

The clinical pictures varied widely, depending to a great extent on the basic pathologic process. Furthermore, the site of the extravasation alters the symptoms, contingent on its extraperitoneal or intraperitoneal position.

TABLE 2.—*Mortality in Spontaneous Rupture* *

| | 1279-1899 | | | 1900-1929 | | |
|---|---|---|---|---|---|---|
| Type | Treatment | Cured | Dead | Treatment | Cured | Dead |
| Intraperitoneal | None | .. | 1 | None | .. | 2 |
| | Laparotomy, rent repaired, no bladder drainage | .. | 1 | Laparotomy, rent repaired, no bladder drainage | 5 | 2 |
| | Laparotomy, rent repaired, urethral drainage | 1 | 1 | Cystotomy only, rent repaired, urethral drainage | 1 | 1 |
| | Medicinal | .. | 7 | | | |
| | Bladder drained by rectal puncture | .. | 1 | | | |
| | Totals | 1 | 12 | Totals | 6 | 5 |
| | Mortality, 92.3% | | | Mortality, 45.4% | | |
| Extraperitoneal | None | .. | 1 | None | 1 | .. |
| | Perineal section | .. | 1 | Cystotomy, perivesical, drainage rent unrepaired | 2 | .. |
| | Perineal section, bladder drainage through rent | 1 | .. | Same, but rent repaired | 2 | .. |
| | Catheter drainage only | 1 | .. | Cystotomy only | 1 | .. |
| | Cystotomy, perivesical drainage | 1 | 1 | Perineal section, drained through the rent | 1 | .. |
| | Totals | 3 | 3 | Totals | 7 | 0 |
| | Mortality, 50% | | | Mortality, 0% | | |
| | Totals | 4 | 15 | Totals | 13 | 5 |
| | Mortality, 78.9% | | | Mortality, 27.2% | | |

* Unless specified to the contrary "laparotomy" and "cystotomy" imply drainage.

In the intraperitoneal type, there is a history of chronic or more frequently acute retention with the sudden onset of severe lower abdominal pain during attempted micturition, defecation or other effort that may cause a sharp rise in intra-abdominal pressure. The history often contains the statement that at the time the patient "felt something give." The patients are often "in shock" when first seen by the physician, or seriously ill, and present the picture of an "acute abdominal condition." The intestines are distended and the abdominal wall is spastic and rigid from peritoneal irritation. Not infrequently shifting dulness may be demonstrated in the flanks.

The onset of the actual rupture in the extraperitoneal extravasation is usually insidious. The patients are not seen by the consultant at the hospital until several days have intervened. At this time they present

the picture of sepsis. There is tenderness and edema above the pubes, or it may be made out by vaginal examination in the female or rectal examination in the male around the base of the bladder or in the lateral aspects of the space of Retzius. Pedersen has called attention to a faint blush and tenderness about the umbilicus which may occur as early as the sixth hour after rupture.

The demonstration of the presence of a rupture was well conceived seven centuries ago and is still in use. The patient is catheterized. If a little blood-stained urine or if none is obtained, rupture is suspected. A measured amount of sterile solution is then injected through the catheter, and the amount of the return flow is noted. If only a little or none returns, it is assumed that the bladder is ruptured. Keen presented the next advance in diagnosis, which consisted of the injection of air instead of fluids in conjunction with the use of the x-rays. In more recent years, the cystoscope has been of definite diagnostic aid when extraperitoneal rupture is suspected. That the method is not harmful and may actually have some therapeutic effect, is demonstrated by the case reported here. When cystoscopy is contraindicated, as in extremely ill patients, or where intraperitoneal rupture is suspected, I should like to suggest the use of iodized poppy seed oil 40 per cent injected into the bladder, although I have not had the opportunity to use it in this connection. But some experience with its use in making hysterosalpingograms convinces me that the oil is not only nonirritating to the peritoneum, but is actually a mild antiseptic, as shown by improvement in cases of low grade chronic salpingitis after its use. The clearcut roentgenogram that it gives would certainly be a great aid to visualization of the existing conditions before operation is attempted.

## TREATMENT

Within the last fifteen years, considerable advance has been made in the standardization of the operative technic for the treatment of rupture of the bladder. In all types, save the rare exception, the operative procedure is an emergency measure to be carried out as soon as the diagnosis is established.

The first operation for the relief of rupture of the bladder found recorded in the available literature was performed in a case in which paracentesis and insertion of an indwelling urethral catheter was done by Cusack in 1814. The patient died in eight days. Harrison did a paracentesis in 1836, and the patient died in forty-two hours. William Walker of Boston performed the first suprapubic cystotomy in a case of extraperitoneal traumatic rupture in 1845. Both the bladder and the space of Retzius were drained, and the patient recovered. In 1861, Walters of Pittsburgh operated in a similar case ten hours after the

accident. The space of Retzius was opened and drained. Urethral drainage of the bladder was established, but no attempt was made to sew the rent. The patient recovered. The first laparotomy with suture of the bladder hole was done by Willet in 1876; Heath reported a case in which similar treatment was done in 1879; Bull of New York, in 1885, and McGill of Leeds, in 1886, employed similar procedures, all with fatal results.

All these operations ignored the prime requisite for success, which is adequate drainage of the bladder. In the intraperitoneal type, the abdomen should be opened and efficient abdominal drainage provided. The abdominal cavity should not be flushed out, simply drained. There is no necessity for sewing the rent, provided the next essential step is taken; this is cystotomy, with the placing of a large suprapubic bladder drainage tube.

In the extraperitoneal type of rupture, the management of the bladder should invariably entail effective drainage, usually from above, rarely in basal ruptures, from below. There is less unanimity of opinion as to the care of perivesical cellulitis, except that free drainage must in some way be attained. In those cases of rupture near or in the trigone, Fuller advocated the perineal approach with drainage of the bladder through the rent and separate drains in the perivesical space. When the extravasations and inflammation are chiefly anterior or high in the lateral spaces, suprapubic cigaret drains of large caliber and suprapubic bladder drainage should be effective. When the position of the rupture or gravity has caused extensive reaction throughout or chiefly about the base, in addition to the inevitable suprapubic bladder drainage, the cigaret drains in the space of Retzius should be through and through, entering above, passing under the pubic arch and emerging from the perineum.

The opinion is becoming general that given free drainage of the bladder, the repair of the rent is unnecessary.

In the event of the survival of the patient, these emergency measures are merely precursors of such steps as will relieve the basic pathologic process.

## SUMMARY

1. Spontaneous extraperitoneal rupture of the bladder is the least dangerous type of rupture.

2. Injection of iodized oil into the bladder is suggested as a diagnostic measure.

3. Under certain conditions, spontaneous cure may take place.

4. The two cardinal principles in the management of the emergency phase of such cases are: (*a*) adequate drainage of the bladder, and (*b*) adequate drainage of the space of Retzius.

## BIBLIOGRAPHY

Symbols: * Traumatic; † spontaneous; ‡ obstetrical; " traumatic and spontaneous.

Alexander, S.: Ann. Surg. **34**:209, 1901.*
Aloi, V.: Riforma med. **37**:851, 1921.*
Angevin, R. W.: Boston M. & J. **179**:100, 1918.*
Ashurst, J.: Ann. Surg. **28**:385, 1898;* Am. J. M. Sc. **132**:17, 1906.*
Beck: Amtl. Ber. ü. d. Versamml. deutsch. Naturf. u. Aerzte **56**:170, 1884.*
Bensaude, R.; Cain, A., and Hillemand, P.: Ann. d. méd. **13**:547, 1923.†
Bedingfield, J.: Lancet **2**:371, 1837.*
Besley, F. G.: Surg. Gynec. Obst. **4**:514, 1907.†
Birkett, J., in Holmes: System of Surgery, London, Parker, Son & Bourn, 1861, vol. 2, p. 480."
Blumer, W. P.: Brit. M. J. **2**:1772, 1900.*
Blundell, J.: Principles and Practice of Obstetric Medicine, Lee & Rogers, 1840, p. 862.‡
Boyer: Malad. chir. **9**:61, 1831.*
Briddon, C. K.: Ann. Surg. **22**:706, 1895; Med. Rec., 1889, p. 278.*
Brown: Med. Rec. **33**:279, 1888.*
Brown, W. H., and McGill: Lancet **2**:971, 1886."
Bryant, J. D.: Med. Rec. **37**:229, 1890.*
Bull, W. T.: Ann. Surg. **1**:67, 1885.*
Bush, J. E.: West. J. Med. & Phys. Sc. **4**:194, 1831.*
Cabot, A. T.: Boston M. & S. J. **125**:396, 1891.†
Caulk, J. R.: J. Urol. **19**:603, 1928; Tr. Am. A. Genito-Urin. Surg. **20**:323, 1927.*
Celdowitch: Arch. f. klin. Chir. **72**:859, 1903.*
Chaldecott, W.: Prov. M. & S. J. **3**:333, 1846.*
Chabourau, G.: Des ruptures de la vessie dans leur rapports avec les fractures du bassin, 1878, Paris.*
Chattaway and Graham: Lancet **2**:754, 1921.*
Civiale, Jean: Traité pratique sur les maladies des organes génito-urinaires, Paris, 1812, p. 261.*
Clark, J. B.: Ann. Surg. **60**:717, 1914.*
Cloquet, J.: North American M. & S. J., vol. 5; London M. & Phys. J., Sept., 1828.*
Coats, J.: Brit. M. J. **2**:121, 1894."
Cooper, B. B.: Guys Hosp. Rep. **2**:488, 1844; London M. Gaz. **1**:844, 1845.*
Cooper, C.: Hot Springs M. J. **10**:227, 1901.*
Courty, L.: Bull. et mém. Soc. de Chir. de Paris **48**:632, 1922.*
Crosbie, A. H.: J. Urol. **12**:443, 1925.†
Cusack, J. W.: Dublin Hosp. Rep. **2**:312, 1818.*
Dalziel: Glasgow M. J. **49**:370, 1898.*
Daubin, C., and Papin, E.: J. d'urol., Paris, 1904.*
Degen: München. med. Wchnschr. **43**:72, 1896.*
Dewar, A.: Edinburgh M. & S. J. **31**:86, 1829.*
Dietrich, R.: Deutsche med. Wchnschr. **48**:974, 1922.*
Ellis, A.: Lancet **1**:20, 1835.*
Engstad: Northwest Lancet **19**:134, 1899.*
Ewebank, in Bell: Diseases of the Urethra, London, 1822, pp. 404 and 437.*
Feré: Progrès méd. **5**:890, 1877.*
Ferraton, L. J. B.: Des ruptures intrapéritonéales de la vessie, Paris, 1883, no. 173*.
Fix, E. N.: Philadelphia M. & S. J., vol. 9.†

Flower, N.: Brit. M. J. **2**:398, 1914.*
Fox, J. M.: Med. News **51**:673, 1887.†
Fraser, L.: Brit. M. J. **1**:921, 1906."
Frieberg, T.: Virchows Arch. f. path. Anat. **202**:268, 1910.†
Fuller, E.: Rupture of the Bladder, J. A. M. A. **63**:2114 (Dec. 12) 1914.*
Galaktionow, A.: Deutsche Ztschr. f. Chir. **110**:449, 1911.*
Gamack: Med.-Chir. Rev., vol. 13.*
Gaume: Paris chir. **13**:272, 1921.‡
Geisinger, J. F.: Ann. Surg. **77**:206, 1923.†
Goldenberg, T.: Beitr. z. klin. Chir. **61**:350, 1909.*
Gordon, L.: Brit. J. Surg. **9**:572, 1922.*
Grant, H. H.: Intraperitoneal Rupture of the Bladder, J. A. M. A. **11**:118 (July 28) 1888.*
Gross, G.: Rev. méd. de l'Est., Aug. 15, 1901.*
Guibal, P.: J. d'urol. **15**:265, 1923.*
Halstrom: Lancet, June 28, 1888.*
Hancock, J. H.: Internat. J. Surg. **36**:146, 1923.*
Hamilton, J.: Dublin Quart. J. M. Sc. **2**:532, 1846.*
Harrison, R.: Dublin J. M. & Chem. Sc. **9**:349, 1836.*
Hawkes, C. E.: Ann. Surg. **65**:222, 1917.*
Heath, C.: Med.-Chir. Tr., London **52**:335, 1879.*
Heaton, G.: Lancet **1**:991, 1896;* Ann. Surg. **5**:455, 1887.*
Herrick, J. B.: North American Pract. **1**:408, 1889;* Med. News **62**:197, 1893."
Heubner: Berl. klin. Wchnschr., Nov. 30, 1899.*
Hewitt, J. B.: London M. Gaz. **10**:733, 1850;* Tr. Path. Soc. London **1**:152, 1850.*
Hey: Med. Obs., Soc. Phys., London **4**:58, 1771.‡
Hiley, J. S.: Lancet **2**:223, 1841.*
Hird: Lancet **2**:480, 1846.*
Hitchcock, H. O.: Pittsburgh M. Rev. **2**:55, 1888.†
Hofmokl: Wien. med. Presse **27**:1196, 1886.*
Holmes, T. H.: Lancet **2**:153, 1887.*
Home, E.: Practical Observation on Treatment of Strictures, London, 1803, vol. 7, p. 230.†
Hoseman: Centralbl. f. chir. **39**:1323, 1912.*
Hulke: Lancet **2**:197, 1892.*
Johnstone, J.: Mem. M. Soc., London **3**:543, 1773.†
Jones, A. T.: Rhode Island M. J. **5**:186, 1922.*
Jones, F.: Ann. Surg. **37**:215, 1903.†
Jonquan: Paris chir., 1909.‡
Katzenstein, M., and Rosen, M.: Ztschr. f. urol. Chir. **12**:310, 1923.*
Keal, W. T.: London M. Gaz. **19**:621, 1836-1837.*
Keefe, J. W.: Am. J. Obst. **47**:84, 1903.*
Keen, W. W.: Ann. Surg. **12**:35, 1890.*
Keenan, C. B.: Canadian M. A. J. **11**:459, 1921.†
Kerr, J.: Ann. Surg. **17**:781, 1887.*
King, W.: Guys Hosp. Rep. **2**:508, 1837.†
Kneeland, J.: New York J. Med. **6**:168, 1851.*
Knight: New Zealand M. J. **3**:158, 1889-1890.*
Koklman, W.: New Orleans M. & S. J. **72**:47, 1919-1920.*
Lane, W. A.: Lancet **1**:867, 1892.*

Larrey, Baron: Surgical Memories of the Campaign in Russia, Germany, France, Trans. from the French by John C. Mercer, Carey, Lee, 1832, p. 180.*
Lavenant and Nagel: Paris chir. **75**:1133, 1916.‡
Lawrence, W.: London M. Gaz. **1**:663, 1839.*
Lawson, C. B.: J. Roy. Army Med. Corps, London **10**:638, 1908.*
Lee, R.: Med.-Chir. Tr., London, vol. 19, p. 238; 1835.†
Lente, F. D.: New York J. Med. **4**:286, 1850.*
Littlewood, H.: Lancet **2**:868, 1898.*
Lloyd, P. A.: Lancet **1**:306, 1892.*
Lynn: Med. Observ. & Inquirer, vol. 4.†
MacCormac, W.: Lancet **2**:1118, 1886; Brit. M. J., May 14, 1887.*
Macewen, W. A.: Lancet **2**:448, 1873.†
McKenna, C. M.: J. Urol. **13**:443, 1925.*
Macpherson, E. M., and Dixon, J.: Med.-Chir. Tr., London **33**:197, 1850.*
Malcolm, R. B.: Canada M. A. J. **15**:1151, 1925.*
Marnock, J.: Ann. Surg. **43**:241, 1906.*
Marsh, H.: Lancet **1**:413, 1893.*
Miginiac, G.: Bull. et mém. Soc. de chir. de Paris **48**:1166, 1922.*
Mikulicz: Deutsche Ztschr. f. Chir. **31**:350, 1890.*
Miles: Med.-Chir. Tr., London **77**:286, 1895.*
Montague, C.: Medical Communications, London, 1790, p. 284.*
Mord, M. J.: Ann. d. mal. d. org. génito-urin. **24**:11, 1906.*
Morris, H.: Proc. Roy. M. & Chir. Soc., London **2**:201, 1885-1887.*
Morrison, R.: Brit. M. J. **1**:191, 1883.†
Moser, E.: Deutsche Ztschr. f. Chir. **132**:103, 1914.*
Negly, J. C.: J. Urol. **20**:307, 1927.†
Nicolaysen, N. A.: Acta chir. Scandinav. **54**:507, 1921-1922.*
Oehlecker, F.: Deutsche med. Wchnschr. **38**:2302, 1912.*
Page: Lancet **1**:887, 1892.*
Partridge: Tr. Path. Soc., London **5**:194, 1853.*
Peaslee, E. R.: Am. J. M. Sc. **19**:383, 1850.*
Pedersen, J.: Tr. Am. Urol. A. **7**:266, 1913."
Pendelton, E. M.: Charleston M. J. & Rev. **5**:456, 1850.*
Percival: Brit. M. J. **1**:1282, 1897.*
Pierus: Historia Anatomico-Medica par Lieutaud, Lib. Primias, 1279, sec. 12, art. 6.†
Pilcher: Ann. Surg., 1893, p. 653.*
Plisson, L.: Lyon chir. **19**:535, 1922.*
Poucher, J. W.: Am. J. Obst. & Gynec. **1**:371, 1921.*
Pridham, F. C.: Brit. M. J. **2**:477, 1927.†
Quain: Lancet **2**:348, 1865.*
Quain, E. P.: Surg. Gynec. Obst. **23**:55, 1916.†
Quick, A. R.: Ann. Surg. **45**:94, 1907.*
Ramsbotham, H. F.: Practical Observations in Midwifery, ed. 2, 1842, p. 146."
Rawson, T. E.: Lancet **1**:253, 1843-1844.
Rhynd, F.: Pathology and Practical Observations on Strictures, 1849, p. 48.*
Rivington, W.: Med. Press & Circ. **35**:157, 1883; **34**:434, 1882; * Ruptures of the Urinary Bladder, London, 1884; * Hunterian Lecture, 1882."
Ryan: Australian M. Gaz. **15**:462, 1896.†
Schlange, H.: Arch. f. klin. Chir. **43**:31, 1892.*
Schuman: Philadelphia M. J., January, 1903.*
Scott: London M. Rep., vol. 17, 1816; † Lancet **1**:387, 1844.*

Shramm: Wien. med. Wchnschr. **33**:1413, 1890.*
Shubert, G.: Beitr. z. klin. Chir. **129**:454, 1923.*
Singer, M.: New York M. Rec., 1888.*
Sims, G. K.: Spontaneous Healing in a Vesico-Uterine Fistula Following Labor, J. A. M. A. **90**:759 (March 10) 1928.†
Smith, R. W.: Dublin Quart. J. M. Sc. **25**:176, 1844.*
Smith, S.: New York J. Med. **6**:336, 1851."
Solly, S.: London M. Gaz., April 26, 1850.*
Sonnenburg, E.: Centralbl. f. Chir., 1855, p. 838.*
South, J. F.: St. Thomas' Hosp. Rep., 1836, vol. 1.*
Stapleton, M. H.: Dublin Quart. J. Med. **9**:217, 1850.*
von Staubenrauch, L.: Arch. f. klin. Chir. **51**:386, 1895.*
Staunton, H. F.: Indian M. Gaz., January, 1889, p. 25.*
Sugetinow: Centralbl. f. Krankh. d. Harn-u. Sex.-Org., 1900, p. 582.†
Symes, S.: London & Edinburgh Month. J. M. Sc. **3**:498, 1843; * Edinburgh M. & S. J., 1848.*
Symonds, C. J.: Lancet **1**:977, 1888.*
Talboy: Iowa M. J. **15**:315, 1908-1909.*
Taylor, A. S.: A Manual of Medical Jurisprudence, Am. ed., Philadelphia, Lea Brothers & Company, 1897, pp. 284 and 287.*
Témoin: Compt. rend. Soc. d'obst. de gynéc. et de pédiat. de Paris **40**:349, 1909.*
Thomas, T. T.: Ann. Surg. **86**:64, 1922.*
von Thompson, H.: Zentralbl. f. Gynäk. **48**:2566, 1924.‡
Thorndike, P.: J. Cutan. Genito-Urin. Dis. **17**:210, 1899.*
Ullmann, E.: Wien. med. Wchnschr. **37**:740, 1887.*
Verstraeten, C.: Ann. Soc. de méd. de Gand. **54**:106, 1876.‡
Vreeland: New York J. Med. **5**:204, 1850.*
Wagner: Arch. f. klin. Chir. **44**:303, 1822.*
Walker, W. J.: Med. Communications to Massachusetts Med. Soc., vol. 2, art 4.*
Walsham, W. J.: Med.-Chir. Tr., London **71**:149, 1888;* Brit. M. J. **1**:191, 1888.*
——and Miles, W.: Med.-Chir. Tr., London **78**:275, 1895."
Walter, A. G.: Med. & Surg. Reporter **7**:153, 1862.*
Ward, J. E.: New York Lancet **1**:78, 1842.*
Waterhouse: Virchows Arch. f. path. Anat., 1890, vol. 119.*
Watson, E.: Month. J. M. Sc. **4**:376, 1848-1849.*
Wells, T. S.: London M. Gaz. **1**:621, 1845.*
White, S., and Wigram, N. J.: Brit. J. Surg. **4**:324, 1916.†
Wigner: Langenbeck's Arch. f. klin. Chir., 1876, vol. 20.*
Willett, A.: St. Barth. Hosp. Rep. **12**:209, 1876.*
Zachariae, P.: Hospitalstid. **65**:293, 1922.*
Zweifel, P.: Monatschr. f. Geburtsh. u. Gynäk. **53**:3, 1920.†

# THE CAUSE OF DEATH IN ACUTE DIFFUSE PERITONITIS *

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Of the several current conceptions regarding the cause of death in acute diffuse peritonitis, that of toxemia is the most commonly accepted. Until 1926,[1] no experimental evidence was offered to substantiate such a conception. Ecker and I [2] were able to produce the death of rabbits following the intraperitoneal injection of broth cultures of *B. coli*. The rabbits that received colon bacillus antiserum intravenously, in addition to the broth culture of colon bacillus intraperitoneally, survived. However, it was later demonstrated [3] that introduction of broth cultures of colon bacillus into the peritoneal cavity of rabbits and dogs may result in the death of the animals, but not necessarily in peritonitis. Since the inflammatory peritoneal lesion was either absent or doubtful and the value of the colon bacillus antiserum is still questioned, the experiments of Ecker and myself are merely suggestive but are by no means conclusive of a bacterial toxin being responsible for death in peritonitis. The second experimental evidence was offered by Williams,[4] who administered *B. welchii* antitoxin to patients with clinical evidences of a severe peritonitis. Williams obtained a large percentage of survivals in patients thus treated. He found a proliferation of *B. welchii* in the small intestine of patients with a low intestinal obstruction and a similar picture in the small bowel of dogs with an experimentally obstructed bowel. Williams hypothecated that death in intestinal obstruction and peritonitis was at least partly due to the absorption of *B. welchii* toxin from the stagnant small bowel. Again, the experiments are suggestive

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1. Steinberg, B., and Ecker, E. E.: The Effect of Antiserum Against the Soluble Toxic Substance of Bacillus Coli in Bacillus Coli Peritonitis, J. Exper. Med. **43**:443 (April) 1926. Williams, B. W.: Peritonitis: The Importance of Toxemia Due to Anaerobic Organisms in Intestinal Obstruction, Brit. J. Surg. **14**:295 (Oct.) 1926.

2. Steinberg and Ecker (footnote 1, first reference).

3. Steinberg, B.: Drainage of the Thoracic Duct in Experimental Peritonitis, J. Exper. Med. **42**:83 (July) 1925.

4. Williams (footnote 1, second reference).

but are inconclusive. The patients might have recovered without treatment with *B. welchii* antitoxin. Furthermore, Williams' patients had peritonitis secondary to intestinal obstruction, and consequently, other factors may be present that are not found in primary peritonitis.

The nature of the toxic action is a matter of much speculation. The theory that a bacterial toxic substance paralyzes the medullary vascular centers has received an additional stimulus by the work of Manenkow.[5] This investigator injected cultures of staphylococcus into the serosa of the stomach of rabbits with a resulting diffuse peritonitis and death of the animals. Similar amounts of a culture of staphylococcus introduced into the serosa of the colon resulted in a localized peritonitis and survival or prolongation of the life of the animals. Manenkow assumed that since the stomach has a direct nerve-lymphatic connection, death was due to the passage of the toxin along the lymphatics of the nerve with the subsequent action on the medullary centers. Kirschner[6] pointed out that the fall in blood pressure in peritonitis occurs only a short time before death, and hence he doubts that the medullary vascular centers are affected by the toxins. Among other theories for which there is little or no evidence there is one which assumes that the toxin acts on the capillaries of the peritoneal cavity with injury and stagnation of the portal circulation.[6] The conception that the intestinal paralysis is a deciding factor in the fatal outcome in diffuse peritonitis is receiving some consideration at present. Askanazy[7] expressed the belief that the intestinal lymphatics dilate, press on the ganglion cells with a consequent paralysis of the intestines. Lennander[8] agreed to the existence of intestinal paralysis and added that the passage of toxins and bacteria through the paralyzed bowel is responsible for death. As a result of a study of the chemical changes of the blood in intestinal obstruction and peritonitis, Orr and Haden[9] stated that there has not been sufficient evidence to justify the belief that intestinal obstruction is alone the cause of death in peritonitis.

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5. Manenkow, P.: Experimentelle Befunde zur Frage des Mechanismus einer direkten Affektion der Oblongata bie diffuser Peritonitis, Ztschr. f. d. ges. exper. Med. **64**:239, 1929.

6. Kirschner: Die Behandlung der eitrigen, freien Bauchfellentzuendung, 50 Tag. d. deutsch. ges. f. Chir. Berlin, 1926; quoted in the Internat. Abstract Surg. **44**:276 (April) 1927.

7. Askanazy, quoted by Heineke, H.: Experimentelle Untersuchungen über die Todesursache bei Perforationsperitonitis, Deutsches Arch. f. klin. Med. **49**:429, 1900-1901.

8. Lennander, quoted in Kaufmann: Lehrbuch der pathologischen Anatomie, trans. by Reimann, Philadelphia, P. Blakiston's Son & Company, 1929, vol. 2, p. 865.

9. Orr, T. G., and Haden, R. L.: Enterostomy in the Treatment of General Peritonitis, Arch. Surg. **18**:2159 (May) 1929.

It is necessary to differentiate between two conceptions regarding the origin of the toxin that is assumed to produce death. One group of workers [10] believed that the toxic action is due to the toxins elaborated in the peritoneal cavity by the bacteria that had produced the peritoneal inflammatory lesion. The other group [11] is of the opinion that the fatal outcome is due to the toxins elaborated by bacteria within the bowel. With intestinal paralysis and stagnation, the toxins are absorbed or pass through the intestinal wall and into the circulation. However, no experimental evidence or sufficient clinical data has been brought forth to demonstrate that there is invariably an intestinal paralysis associated with a fatal outcome in diffuse peritonitis.

## EXPERIMENTAL WORK

The following experiments were undertaken: (1) to ascertain the rôle of bacterial toxins in the outcome of diffuse peritonitis; (2) to determine the type of toxin (from the bacteria within the bowel or from bacteria within the peritoneal cavity) responsible for death; (3) to learn the effect of the toxins on the cellular reaction of the peripheral blood and that evoked in the peritoneal cavity. In order to accomplish these purposes, it was necessary to choose a micro-organism that is not found in the intestinal contents, that is a definite toxin producer and possesses a recognized antitoxin, and that is capable of producing invariably a fatal diffuse peritonitis in a laboratory animal. The diphtheria bacillus answered all these requirements.

In order to determine the effect of diphtheria toxin [12] on dogs, ten of these animals were given injections of varying amounts of toxin (from 0.5 to 2 cc.) intravenously, subcutaneously or intraperitoneally. The animals died in from eighteen to forty-eight hours after the injection of the toxin.

Production of experimental fatal peritonitis by known and controlled agents had met with difficulties in the hands of many investigators. The methods employed usually accomplished only a part of the required purpose. On the introduction of the agent, the animal died but had no peritoneal inflammation, or if a peritonitis was produced, the animal survived. Other methods that induced both the local peritoneal lesion and death produced these results only in a small and varying percentage of the experimental animals, and the methods employed contained unknown and uncontrollable agents. A procedure that fails to secure (in 10 per cent of animals) a definite peritonitis resulting in death lacks

10. Steinberg and Ecker (footnote 1, first reference). Manenkow (footnote 5). Kirschner (footnote 6).

11. Williams (footnote 1, second reference). Askanazy (footnote 8).

12. The diphtheria toxin was obtained from the laboratories of the New York State Department of Health through Miss Mary B. Kirkbride.

the essential requirements of a properly controlled experiment. A suggestion of a method that invariably results in a fatal peritonitis was made by Benians.[13] He injected intraperitoneally into rabbits colon bacilli suspended in gum tragacanth. This procedure was later adopted for dogs and repeatedly confirmed.[14]

The principle of the method of Benians was adopted in these experiments. The saline washings of three blood agar slants of a twenty-four hour culture of diphtheria bacilli were suspended in a 2.5 per cent saline suspension of gum tragacanth and injected by means of needle and syringe through the abdominal wall into the peritoneal cavity of dogs.[15] At the onset of the experiments, thirteen animals and later nine additional dogs, were given injections of this material. The twenty-two animals died in from eighteen to forty-eight hours of a severe fibrinopurulent hemorrhagic peritonitis.

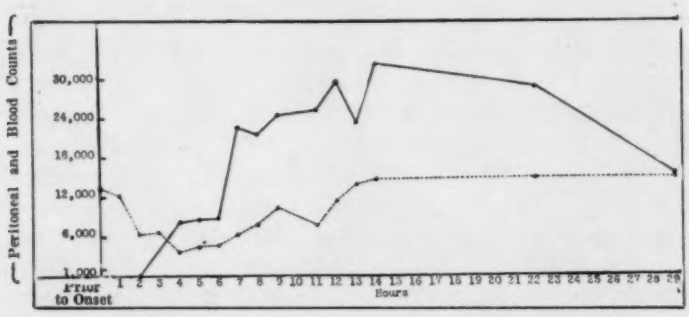


Chart 1.—Blood counts and peritoneal counts in a normal dog given injections intraperitoneally with three slants of diphtheria bacilli in gum tragacanth. The animal died. In this and the following charts the dotted line indicates the blood counts and the unbroken line the peritoneal counts.

It was assumed that if death of the twenty-two animals was due to the toxin liberated by the diphtheria bacilli, diphtheria antitoxin in sufficient amounts would neutralize the toxin and avoid death. To test this assumption, each of fifteen dogs were given injections intraperi-

13. Benians, T. H. C.: Further Experiments with Fixation Areas, Bearing on Pathogenicity of Bacillus Coli in Peritoneal Infections, Brit. J. Exper. Path. **5**:123 (June) 1924.

14. Steinberg, B., and Goldblatt, H.: Studies on Peritonitis: II. Passage of Bacteria from the Peritoneal Cavity into Lymph and Blood, Arch. Int. Med. **39**: 449 (March) 1927. Goldblatt, H., and Steinberg, B.: Peritonitis, Active Immunization Against Experimental B. Coli Peritonitis, ibid. **41**:42 (Jan.) 1928. Steinberg (footnote 3).

15. It was found that a suspension of one slant injected into a dog weighing 10 Kg. invariably resulted in a fatal peritonitis.

toneally of the saline washings of three slants of a twenty-four hour culture of diphtheria bacilli suspended in 2.5 per cent gum tragacanth, and at the same time diphtheria antitoxin was administered by the routes indicated in table 1. (These fifteen dogs received the intraperitoneal injection at the same time as the first set of the thirteen control dogs.) All of the fifteen dogs that were given diphtheria antitoxin survived. The animals were slightly ill during the first eighteen hours but after that they were apparently well.

It was demonstrated previously [16] that when bacteria (colon bacilli) are suspended in gum tragacanth and injected into the peritoneal cavity of dogs, the bacteria remain almost entirely in the peritoneal cavity. There is no passage of the micro-organisms into the circulation, and hence whatever struggle occurs between the defenses of the body and the invading bacteria takes place in the peritoneal cavity. Snyder and

TABLE 1.—*Effect of Diphtheria Antitoxin on Dogs in Which Peritonitis Has Been Produced by Diphtheria Bacilli*

| No. of Dogs | Type of Material Injected Intraperitoneally | Units of Diphtheria Antitoxin Given | Route of Administration of Antitoxin | Outcome |
|---|---|---|---|---|
| 13<br>9 | Three slants of diphtheria bacilli in 40 cc. of a 2.5% suspension of gum tragacanth | None | ..... | Died in from 18 to 48 hours with a marked hemorrhagic peritonitis |
| 11 | Three slants of diphtheria bacilli in 40 cc. of a 2.5% suspension of gum tragacanth | 20,000 | Intravenously | Survived |
| 2 | Three slants of diphtheria bacilli in 40 cc. of a 2.5% suspension of gum tragacanth | 20,000 | Intramuscularly | Survived |
| 1 | Three slants of diphtheria bacilli in 40 cc. of a 2.5% suspension of gum tragacanth | 20,000 | Intraperitoneally | Survived |
| 1 | Three slants of diphtheria bacilli in 40 cc. of a 2.5% suspension of gum tragacanth | 20,000 | Subcutaneously | Survived |

I [17] took advantage of this observation to study the cellular reactions within the peritoneal cavity during the course of peritonitis. From these studies, it was determined that polymorphonuclears constitute the first line of cellular defense and that bacterial phagocytosis by the polymorphonuclears represents the primary and the conspicuous cellular protective reaction on the part of the body.

In order to ascertain the rôle played by the polymorphonuclears and phagocytosis in the animals passively immunized with diphtheria antitoxin, a study more or less similar to that by Snyder and myself was made in these experiments. Total and differential white cell counts of

16. Steinberg and Goldblatt (footnote 14, first reference).

17. Steinberg, B., and Snyder, D. A.: Immune Cellular Reactions in Experimental Peritonitis, Arch. Path. **8**:419 (Sept.) 1929.

the peritoneal and peripheral blood were made at short intervals. Peritoneal counts were done by introducing glass capillary pipets through the abdominal wall under sterile conditions and withdrawing the peritoneal fluid. At frequent intervals bacterial counts were made on the peritoneal exudate. The peritoneal, the peripheral cell and the bacterial counts were performed on a normal dog that received by intraperitoneal injection three slants of diphtheria bacilli in 2.5 per cent gum tragacanth to serve as a control for the observations in the passively immunized animal.

In both animals (the control and the passively immunized dog) there was an initial drop of the peripheral white cell count and an

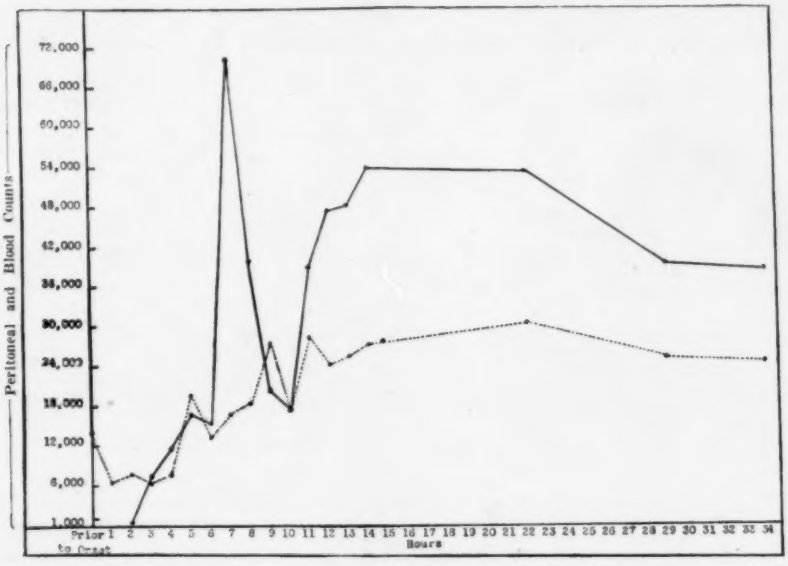


Chart 2.—Blood counts and peritoneal counts in a normal dog given injections intraperitoneally of three slants of diphtheria bacilli in gum tragacanth and injections intravenously of diphtheria antitoxin. The animal survived.

appearance of a small number of cells in the peritoneal exudate. Snyder and I are of the opinion that this initial drop of the total white cells of the blood represents a migration to the inflammatory field and constitutes the first line of cellular defense. There is a gradual rise of the total white cells in the peritoneal cavity of both dogs. The peak of the peritoneal counts in the passively immunized animal is reached at the end of the seventh hour, while in the control dog the peak appears at the end of the fourteenth hour and the total cell count is less than half that of the immune dog (tables 2 and 3; charts 1 and 2). Comparative studies of the peritoneal smears of the control and the

immune dogs (tables 2 and 3) reveal the presence of free bacteria in the exudate of the control dog as late as the eleventh hour (in other control animals, free bacteria were found up to and including the last hour) after the onset of peritonitis, while in the passively immunized dog no free bacteria were seen at the end of the third hour. It was

TABLE 2.—*Blood and Peritoneal Counts in a Normal Dog with Peritonitis Produced by Diphtheria Bacillus*

| | | Differential Blood Count, per Cent | | | | | Differential Peritoneal Count, per Cent | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Hours After Onset of Peritonitis | Blood Count | Polymorphonuclears | Lymphocytes | Monocytes | Eosinophils | Peritoneal Count | Polymorphonuclears | Lymphocytes | Monocytes and Plasmatocytes | Comments on Peritoneal Exudate |
| Before | 13,600 | 79 | 12 | 9 | .. | ..... | .. | .. | .. | |
| 1 | 12,550 | 72 | 21 | 6 | .. | ..... | .. | .. | .. | |
| 2 | 6,500 | 60 | 30 | 7 | 3 | 1,000 | 100 | .. | .. | Many free bacteria; few polymorphonuclears have many bacteria; many red blood cells |
| 3 | 6,700 | 66 | 24 | 7 | .. | No count | 100 | .. | .. | Same as preceding hour |
| 4 | 4,900 | 77 | 16 | 6 | 1 | 8,150 | 94 | 3 | 3 | 13,200,000 bacteria per cc.; few free bacteria, most of them phagocytosed |
| 5 | 5,450 | 74 | 22 | 4 | .. | 8,650 | 97 | 1 | 2 | Same as preceding hour |
| 6 | 5,550 | 92 | 4 | 4 | .. | 8,800 | 98 | 2 | .. | 9,600,000 bacteria per cc.; otherwise same as preceding hour |
| 7 | 6,350 | 90 | 5 | 5 | .. | 22,850 | 100 | .. | .. | 5,440,000 bacteria per cc.; occasional free bacterium; many polymorphonuclears with phagocytosed bacteria |
| 8 | 8,000 | 87 | 11 | 2 | .. | 21,900 | 98 | 1 | 1 | No free bacteria; 1 of 30 polymorphonuclears has phagocytosed bacteria; many degenerated polymorphonuclears |
| 9 | 10,300 | 93 | 6 | 1 | .. | 24,400 | 99 | .. | 1 | Same as preceding hour |
| 11 | 7,700 | 87 | 11 | 2 | .. | 25,200 | 98 | .. | 2 | 3,424,000 bacteria per cc.; bacteria are free and clumped |
| 12 | 11,350 | 87 | 12 | 1 | .. | 29,800 | 100 | .. | .. | Same as preceding hour |
| 13 | 14,000 | 84 | 16 | .. | .. | 23,150 | 97 | .. | 3 | 1,840,000 bacteria per cc.; otherwise same as preceding hour |
| 14 | 14,550 | 91 | 5 | 4 | .. | 32,100 | 100 | .. | .. | Many polymorphonuclears with phagocytosed bacteria |
| 22 | 14,900 | 92 | 8 | .. | .. | 28,800 | 100 | .. | .. | Same as preceding hour |
| 29 | 14,950 | 89 | 8 | 3 | .. | 15,050 | 100 | .. | .. | No bacteria on culture, few polymorphonuclears with phagocytosed bacteria; dog died on thirtieth hour |

apparent that in addition to the neutralization of the toxin by the antitoxin there were differences in the rapidity of phagocytosis and the number of polymorphonuclears evoked in the two dogs. The passively immunized dog was capable of a more rapid phagocytosis of the invading bacteria and was also able to muster a large and sufficient number of polymorphonuclears to cope with the micro-organisms. A comparison of charts 2 and 3 of an actively and passively immunized animal shows a close similarity in the reaction. As an illustration of a cellular

response in presence of active immunity, peritonitis was produced by *B. coli* in a dog immunized with *B. coli* (Goldblatt and Steinberg [18]). The differences between the two animals consisted in the earlier appearance (fourth hour) of large numbers of polymorphonuclears and the considerably greater total number of these phagocytes in the actively than in the passively immunized dog. The rapidity of phagocytosis was alike in both animals. Comparing charts 2 and 3 of the two differently immunized dogs with that of a nonimmune animal (table 2),

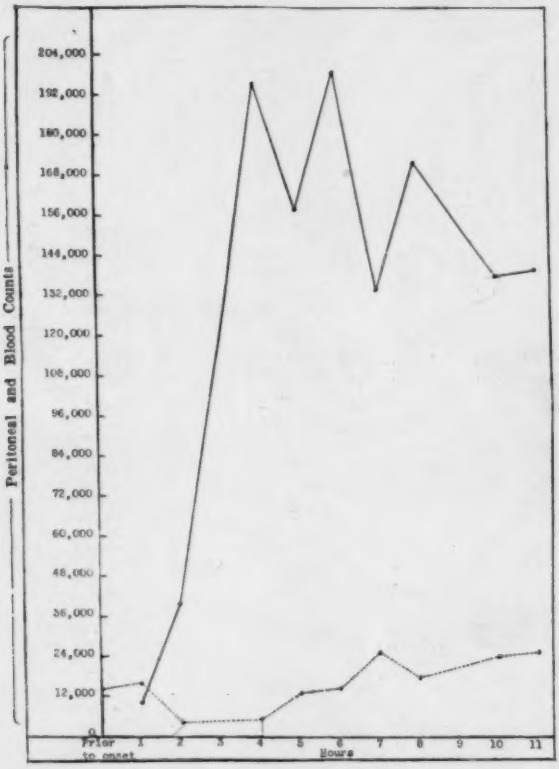


Chart 3.—Blood counts and peritoneal counts in a dog immunized with B. coli and given injections intraperitoneally of two slants of colon bacillus in gum tragacanth. The animal survived.

the differences of the time of appearance and the number of polymorphonuclears are quite apparent. The differences are still more striking in the smears of the peritoneal exudate. From the onset of peritonitis to the death of the nonimmune animal, the slides are filled with viable and free bacteria; all the polymorphonuclears are filled to

18. Goldblatt and Steinberg (footnote 14, second reference).

capacity with bacteria, but there are not enough of these phagocytes to take care of all the micro-organisms. On the other hand, in the slides of the immunized animals there are very few free bacteria at the end of the second hour and none at all at the end of the third hour.

TABLE 3.—*Effect of Diphtheria Antitoxin on Blood and Peritoneal Counts of Normal Dog in Which Peritonitis Has Been Produced with Diphtheria Bacilli*

| | | Differential Blood Count, per Cent | | | | | Differential Peritoneal Count, per Cent | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Hours After Onset of Peritonitis | Blood Count | Polymorphonuclears | Lymphocytes | Monocytes | Eosinophils | Peritoneal Count | Polymorphonuclears | Lymphocytes | Monocytes and Clasmatocytes | Comments on Peritoneal Exudate |
| Before | 14,000 | 70 | 23 | 4 | 3 | ..... | .. | .. | .. | |
| 1 | 6,550 | 76 | 23 | 1 | .. | ..... | .. | .. | .. | |
| 2 | 7,800 | 80 | 18 | 2 | .. | 1,350 | 100 | .. | .. | Bacteria are free and in clumps; polymorphonuclears filled with bacteria |
| 3 | 6,250 | 86 | 10 | 4 | .. | 7,350 | 98 | 2 | .. | No free bacteria; many phagocytosed bacteria; many new polymorphonuclears |
| 4 | 7,950 | 86 | 12 | 2 | .. | 11,950 | 98 | .. | 2 | Many broken down polymorphonuclears |
| 5 | 19,700 | 89 | 9 | 2 | .. | 16,900 | 100 | .. | .. | Same as preceding hour; 3,952,000 bacteria per cc. |
| 6 | 13,100 | 84 | 10 | 4 | 1 | 15,350 | 100 | .. | .. | Few polymorphonuclears with bacteria; none free |
| 7 | 16,900 | 93 | 5 | 2 | .. | 70,400 | 100 | .. | .. | Same as preceding hour; 4,000,000 bacteria |
| 8 | 18,600 | 93 | 7 | .. | .. | 40,000 | 98 | .. | 2 | Degenerated polymorphonuclears with bacteria |
| 9 | 27,200 | 91 | 9 | .. | .. | 20,500 | 100 | .. | .. | Same as preceding hour |
| 10 | 17,400 | 89 | 11 | .. | .. | 17,600 | 99 | 1 | .. | Same as preceding hour |
| 11 | 28,550 | 96 | 4 | .. | .. | 38,950 | 97 | 3 | .. | No bacteria in polymorphonuclears |
| 12 | 24,100 | 96 | 4 | .. | .. | 47,700 | 96 | 2 | 2 | Occasional polymorphonuclears with phagocytosed bacteria; 1,152,000 bacteria per cc. |
| 13 | 25,550 | 96 | 4 | .. | .. | 48,200 | 98 | 2 | .. | Many broken down polymorphonuclears |
| 14 | 27,400 | 99 | 1 | .. | .. | 54,000 | 97 | 3 | .. | Same as preceding hour |
| 22 | 30,600 | 93 | 6 | 1 | .. | 53,500 | 95 | 2 | 3 | No free or phagocytosed bacteria |
| 29 | 25,050 | 96 | 2 | 2 | .. | 39,100 | 95 | 5 | .. | Same as preceding hour |
| 34 | 24,250 | 92 | 4 | 4 | .. | 38,750 | 94 | 4 | 2 | An occasional polymorphonuclear with a phagocytosed bacterium |
| 45 | 21,900 | 94 | 6 | .. | .. | 44,500 | 97 | .. | 3 | Same as preceding hour; no bacterial growth on culture |
| 50 | 21,300 | 92 | 6 | 2 | .. | 27,000 | 90 | .. | 10 | No bacterial growth on culture |
| 52 | 12,800 | 83 | 14 | 3 | .. | 14,600 | 91 | 9 | .. | Same as preceding hour; dog survived |

Since the survival of the animal with acute diffuse peritonitis is coincident with a rapid phagocytosis and the capacity to evoke a sufficiently large number of polymorphonuclears to cope with the invading bacteria, and the experiments reported here demonstrate that a bacterial toxin plays a deciding part in the death of the animal, it is assumed that in the presence of a sufficient number of polymorphonuclears and a rapid

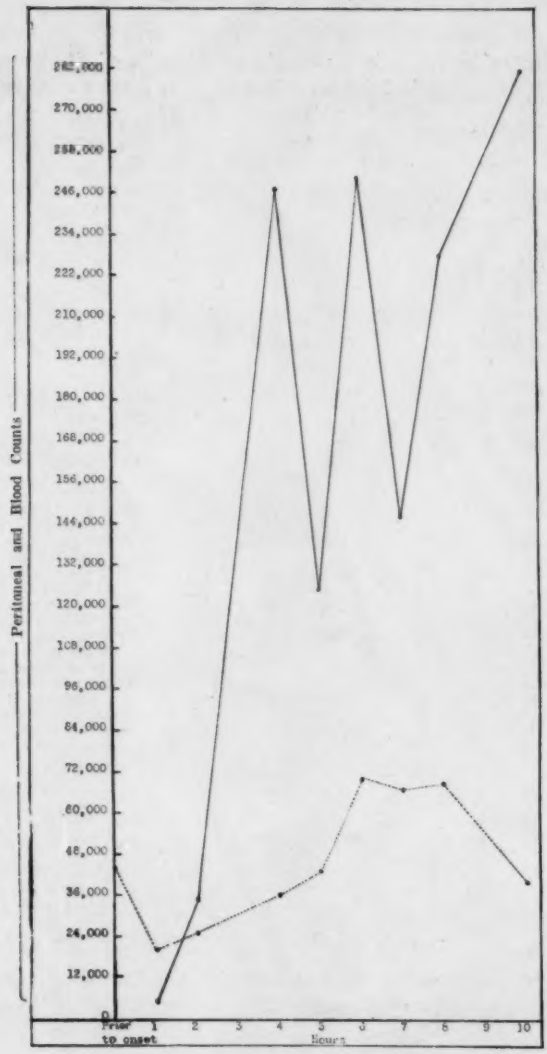


Chart 4.—Blood counts and peritoneal counts in a dog immunized with B. coli and given injection intravenously of two slants of colon bacillus in gum tragacanth and injections intravenously of 2 cc. of diphtheria toxin. The animal died ten and one-half hours after injection.

phagocytosis the elaboration of the toxin by the bacteria within the peritoneal cavity is prevented.

The peritoneal and peripheral leukocytosis in the passively immunized animal suggested that the bacterial toxin may inhibit the production or mobilization of polymorphonuclears. Consequently, the administration of the antitoxin neutralized the toxin and removed the cellular inhibitory factor. A dog was immunized with *B. coli* according to the method of Goldblatt and myself,[18] the animal was later given intraperitoneal injections with two slants of *B. coli* in 40 cc. of a 2.5 per cent suspension of gum tragacanth, and at the same time 2 cc. of diphtheria toxin was administered intravenously. Control dogs that

TABLE 4.—*Results in a Dog Immunized with B. Coli and Given Two Slants of Colon Bacilli in Gum Tragacanth Intraperitoneally and 2 cc. of Diphtheria Toxin Intravenously* *

| Hours After Onset of Peritonitis | Blood Counts | Peritonal Counts | Comments on Peritoneal Exudate |
|---|---|---|---|
| Prior to onset | 44,450 | ..... | |
| 1 | 20,050 | 4,700 | An occasional free bacterium; many phagocytosed bacteria; all cells are polymorphonuclears |
| 2 | 25,550 | 34,750 | Many free and phagocytosed bacteria; all cells are polymorphonuclears |
| 4 | 36,700 | 247,200 | Many free and phagocytosed bacteria; all cells are polymorphonuclears |
| 5 | 43,850 | 125,500 | Few free bacteria; many phagocytosed bacteria; all cells are polymorphonuclears |
| 6 | 70,900 | 250,000 | Few free bacteria; many phagocytosed bacteria; all cells are polymorphonuclears |
| 7 | 67,600 | 146,000 | A moderate number of free bacteria; all cells are polymorphonuclears |
| 8 | 68,800 | 227,750 | Few free bacteria; many phagocytosed bacteria; many broken down polymorphonuclears; all cells are polymorphonuclears |
| 10 | 40,000 | 281,000 | Few free bacteria; many phagocytosed bacteria; many broken down polymorphonuclears; all cells are polymorphonuclears |

* The animal died ten and one-half hours after the injection.

were similarly immunized with *B. coli* and in which a similar peritonitis was produced with colon bacillus, survived. If a bacterial toxin (diphtheria toxin) inhibits polymorphonuclear formation or mobilization, these phagocytes which ordinarily appear in large numbers in immunized animals will either be diminished in number or totally suppressed. The results of this experiment revealed that diphtheria toxin neither diminished nor inhibited the polymorphonuclear response to an acute diffuse infection of the peritoneum (chart 4). The cellular response was as rapid and as great as in the immune animal without diphtheria toxin (chart 3). However, studies of the peritoneal exudate revealed the presence of free and viable (by culture) bacteria from the first to the tenth hour after the onset of peritonitis in the animal given the diphtheria toxin (table 4). On the other hand, many of the bacteria were phagocytosed. This observation may be suggestive of some

inhibitory or deleterious affect on the polymorphonuclear by the bacterial toxin with a consequent slight to moderate interference with the phagocytic property of the polymorphonuclears.

## CONCLUSIONS

In acute diffuse peritonitis, under the conditions of these experiments, death is due to the toxin produced by the bacteria present in the peritoneal cavity. Intestinal paralysis, intestinal stasis and intestinal bacteria, under these conditions, play no part in the death of the animal.

Administration of the corresponding antitoxin averts death in acute diffuse peritonitis.

In the absence of an antitoxin that is capable of neutralizing the toxin, two factors are responsible for the survival of the animal with peritonitis: (1) rapid phagocytosis and (2) a sufficiently large number of polymorphonuclears to cope with the invading bacteria. It is assumed that in the presence of these two factors, the formation of toxin by bacteria is prevented and the death of the animal is averted.

The bacterial toxin has no inhibitory effect on the number or on the rapidity of appearance of the polymorphonuclears. However, the toxin interferes with complete phagocytosis of the bacteria by the polymorphonuclears.

# A REVIEW OF UROLOGIC SURGERY

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## KIDNEY

*Anomalies.*—Braasch [1] observed a number of cases in which the renal pelvis had an anomalous position and form and in some cases was the only clinical evidence of abnormality. When renal anomaly is characterized only by anomalous rotation, the degree of rotation may vary, and may be described by the terms rotation absent, incomplete, reverse and excessive. It does not always involve the entire kidney, but may be confined to one pole and may affect only a segment of the pelvis and the adjacent calices. Although the pelvis may be in the normal position, it is more often observed with either lateral or mesial displacement or with slight ptosis. It is usually situated on a level with the second lumbar vertebra. It may be slightly lower and is then distinguished from ectopic kidney by the fact that its blood vessels take origin at the usual level of the renal artery and vein. It may occur as the result of either congenital or acquired factors; if of congenital etiology, it is referred to as anomalous rotation; if secondary to acquired factors, it is designated as renal torsion.

In fused kidneys, evidence of abnormal rotation is always found, at least in one pelvis, and usually in both. Recognition of fused kidney is made possible largely by demonstration, in the pyelogram, of failure of pelvic rotation. As a result of inability of the fused kidney to rotate, the renal pelves remain situated on the anterior aspect of the kidney. The calices usually extend anteriorly, mesially or laterally, and often are clubbed terminally. The ureteropelvic juncture may be

1. Braasch, W. F.: Anomalous Renal Rotation and Associated Anomalies, J. Urol. **25**:9 (Jan.) 1931.

situated either on the anterior aspect of the pelvis or on its lateral or mesial border.

Failure of the embryonic kidney to make its normal ascent results in congenital renal dystopia or ectopic kidney. The kidney usually is abnormal in structure, and, as a result of failure of rotation, the pelvis is situated anteriorly and is bizarre in outline. The renal blood vessels are usually abnormal in number and arrangement and often influence the anomalous shape and position of the kidney and its pelvis.

The clinical diagnosis of anomalous rotation is possible only by means of pyelography. Evidence of renal rotation may be observed with clinical conditions in which it may be difficult to determine whether the rotation was primary or secondary.

Abnormal rotation of the kidney observed as the result of other than congenital factors is known as renal torsion. It may result from displacement from either extrarenal or intrarenal pathologic conditions, renal ptosis, postoperative deformity and injury. As a result of torsion, the kidney may be displaced in any direction and its axis changed to various angles. The pyelogram usually will reveal pelvic rotation, varying from a slight difference in the axis of one or more calices to complete reversion of the pelvic arrangement. As a result of marked renal ptosis, or from displacement by extrarenal tumor, the renal pelvis may assume a position and contour suggestive of ectopic kidney.

In pyelographic examination occasionally a renal pelvis is observed the shape of which is suggestive of congenital deformity; this is termed an embryonic pelvis. Its outline is characterized by an elongated pelvis, from which a series of abbreviated calices extend laterally, anteriorly or mesially, at comparatively regular intervals. It may be associated with a variable degree of abnormal rotation. Although the kidney is sometimes in a normal position, there may be a variable degree of dystopia, and there is usually some evidence of incomplete rotation. Surgical exploration may reveal that the kidney is abnormal in shape and size; it may be comparatively elongated, and often there is marked evidence of fetal lobulation.

It is known that an anomalous kidney is more often affected by lesions than a normal kidney. Hydronephrosis and stone are the lesions most commonly found and may be the direct results of anomaly. Symptoms suggestive of nephralgia frequently are associated with an anomalous renal position.

Lazarus [2] stated that one of the most common anomalies of the genito-urinary system is that of supernumerary or double ureter. The

2. Lazarus, J. A.: Heminephrectomy for Calculus Pyonephrosis in a Case of Bilateral Duplication of Ureters and Pelves, J. Urol. **24**:503 (Nov.) 1930.

pelves associated with complete reduplication of the ureter are usually of unequal size and configuration. The upper pelvis is the smaller and possesses fewer calices. Although the capacity of the pelves is unequal, the segments usually have equal functional activity. The ureters as they leave the pelves lie close together and are usually connected by strands of connective tissue. They terminate in the lateral trigonal angle in such a way that one ureteral orifice lies just above the other. The upper one corresponds to the lower pelvis and the lower one to the upper pelvis. The upper pelvis is usually the smaller of the two.

Lazarus reported a case of bilateral duplication of the ureters in which heminephrectomy was performed. At operation the kidney was elongated and consisted of two portions separated by a shallow groove running across the anterior surface of the renal mass. The upper portion, which comprised about two thirds of the entire mass, appeared normal and contained a small intrarenal pelvis with a diminutive ureter; the lower third was represented by a pyonephrotic sac containing small calculi with a dilated pelvis and ureter. The blood supply of the lower pole appeared to arise as branches of the main renal pedicle which passed to the upper hilus. These branches coursed downward over the anterior surface of the pelvis to enter the hilus of the sac anterior to the pelvis. After the kidney had been completely mobilized, the ureters were isolated and freed from their adhesions of connective tissue, and the blood supply of the lower renal portion was clearly defined. The vessels were doubly ligated and divided. The dilated ureter was then divided. The lower pyonephrotic portion of the kidney was amputated just above the groove, a good wedge of the healthy kidney being taken with it. Bleeding was brisk, but was easily controlled with clamps and ligatures. Two large strips of muscular tissue were laid across the cut end of the kidney and six mattress sutures were used to close the rent, the tissue being incorporated within them. Following decapsulation, a flap of perirenal fat was loosely stitched over the sutured pole of the kidney, and a rubber tube and dam were placed below this for drainage. The wound was closed about the drains in layers.

The postoperative course was uneventful. At no time was there any urinary leakage. The patient left the hospital on the twenty-third postoperative day with the wound solidly healed.

[COMPILERS' NOTE.—On first thought, resection of the diseased segment of a double kidney seems to be a formidable procedure. When conditions are favorable, however, it offers no great technical difficulties and is followed by favorable results. Heminephrectomy should not be attempted unless the pathologic condition is confined entirely to one segment and clinical evidence shows definitely that the remaining seg-

ment is normal and functioning. Even under such favorable circumstances infection may invade the remaining segment, necessitating a secondary operation. With proper suturing, the postoperative hemorrhage should be negligible. If infection remains in the tissues, however, a sinus may persist indefinitely and reopen at intervals. The healing process resulting after heminephrectomy was clearly shown in a case reported by Braasch and Scholl in which the remaining segment of a double kidney was subsequently removed. The resected surface, although pitted in some areas, was smooth, and had assumed the normal rounded contour of one of the renal poles. The pathologic process had involved only the tissues immediately adjacent to the line of incision. There was moderate lymphocytic infiltration in some areas, possibly caused by absorbed suture materials. The glomeruli were somewhat clumped and the destruction of interglomerular tissue was greater than that of glomeruli. There was only slight fibrosis and hyalinization of the glomeruli, and many immediately adjacent to the line of incision were apparently normal. Factors rendering the operation easier and favorably influencing the results are: (1) the considerable distance separating the two pelves; (2) a definite division of the two segments by a cicatricial band, and definite confinement of the disease to one segment, and (3) the chronic and cicatricial nature of the pathologic lesion.]

Bumpus [3] cited the case of a young woman whose pyelogram, made at the Mayo Clinic in August, 1928, showed evidence of two pelves, one anterior to the other, due to longitudinal instead of transverse division. A pyelogram of the opposite kidney was obtained three days later and indicated that this kidney was normal. The divided functional test showed a 10 per cent return of the dye from each kidney in fifteen minutes.

In Young's experience the pelves of a double kidney are always situated one above the other, the division being transverse, but in the report of a case of duplication of the renal pelvis Potter and Sexton stated that the division may be longitudinal through the kidney with one pelvis anterior and one posterior.

Lafitte [4] observed a case of congenital pelvic kidney during pregnancy. He mentioned that these anomalies are not common, although Girard in 1911 reported 102 cases. They are the most common anomalies of position of the kidney. Congenital pelvic kidney may be situated more or less high, sometimes at the entrance of the small pelvis or

3. Bumpus, H. C., Jr.: Unusual Duplication of Renal Pelvis, J. Urol. **25**:39 (Jan.) 1931.

4. Lafitte: Ectopie pelvienne congénitale du rein observée au cours d'une grossesse, Bull. et mém. Soc. nat. de chir. **56**:910 (July 12) 1930.

entirely in the pelvis itself, being found in the concavity of the sacrum, or it may lie on the pelvic floor. When the kidney lies at the level of the entrance of the pelvis, the organ may constitute a decided obstacle to the ascension of the pregnant uterus and to the normal mechanism of delivery; it may narrow the pelvis more than 3 cm. Such a kidney is usually fixed; it is only partially mobile, which is indicated by possible torsion on its axis. The possibility of fixing it higher has been considered but rejected; it cannot be transported either to the lumbar region or to another situation in the pelvis where its presence would not be such a marked obstacle to normal pregnancy. The value of the corresponding kidney should be estimated. Nephrectomy may be indicated in a few cases. If the kidney is healthy and the pregnancy has advanced two months, Lafitte advised waiting until full term before intervention. In some cases, operation may be carried out just before childbirth. Girard reported a series of cases of pregnancy and ectopic kidney. Four patients were operated on during pregnancy and 9 during labor; abortion occurred in 13 cases. If ectopy was not complete, delivery was spontaneous but painful and prolonged.

[COMPILERS' NOTE.—Ectopic kidneys in general are prone to the development of pathologic states. They may produce dystocia when they lie at or below the pelvic rim. If the uterus has been able to rise above the pelvis into the abdomen and interference with the descent of the fetus at term takes place, the rare indication for cesarean section may arise, particularly if the ectopic kidney is known to be functioning normally. As Girard, quoted by Lafitte, pointed out, abortion will be the most common outcome.]

*Tumors.*—Busser [5] concluded from a study of 94 cases of primary epitheliomas of the kidney that it is impossible to judge the histologic structure of carcinoma of the kidney by its gross appearance. From a macroscopic point of view, carcinomas of the kidney present aspects as follows: a partial nodular form with preservation of some healthy renal tissue; a massive nodular form; rarely, an infiltrated form, and a cystic form, which is always localized at the lower pole. Histologically tumors are divided into two groups, epitheliomas of renal type and undifferentiated epitheliomas. The renal type is tubular and papillary; the undifferentiated type is alveolar and trabecular. Between these two types are found many different transitory types showing the evolution of the first type into the second one. Busser expressed the belief that

5. Busser, F.: Étude anatomique des épithéliomes primitifs du rein chez l'adulte; à propos de 94 observations, Bull. de l'assoc. franç. p. l'étude du cancer **19**:198 (March) 1930.

the theory of the hypernephroma is a fallacious one; all epitheliomas of the kidney are of renal origin.

[COMPILERS' NOTE.—Busser's grouping is somewhat similar to that of Ewing, who divided tumors of the kidney into two main groups, papillary adenocarcinomas and alveolar carcinomas. In a series of cases reported from the Mayo Clinic in which nephrectomy was performed for tumor, the major portion belonged to the first group of papillary adenocarcinomas. These tumors, usually considered as the hypernephroma group, are the most common of renal tumors. As a rule they are only moderately malignant, not infrequently existing for years without causing symptoms. They generally become large, bulky and hemorrhagic, and cause marked distortion of the renal contour. They occurred in 152 (82.5 per cent) of 184 cases. Thirteen (8.5 per cent) of the patients died following operation, 23 were not traced after operation and 57 (53.8 per cent) of the remaining 106 were living and well on an average of six years after operation.

The second group, or alveolar carcinomas, form only a small proportion of renal tumors. They are homogeneous and whitish, and at times diffusely infiltrate the renal tissues. They are highly malignant, early invading the pelvis and breaking through the renal capsule. Hemorrhage and the formation of cysts are rare. Histologically these tumors tend to reproduce the tubules of the adult kidney, resembling the renal parenchyma. The structure varies from that of well formed alveoli to areas in which there is little differentiation, the cells being matted together with only a small amount of intervening stroma. There were 32 cases of alveolar carcinoma in the series. Five (15.6 per cent) of the patients died following operation; 4 patients were not traced, and only 3 (13.4 per cent) of the remaining 23 were still alive. These three patients were living on an average of ten years after nephrectomy.]

Kretschmer and Hibbs[6] studied 17 cases of malignant tumors of the kidney which occurred in infants and children. Such tumors are rare; Bugbee and Wollstein, in a review of 4,903 necropsies on infants and children, did not report a case of malignant renal tumor.

Wilms showed that mixed tumors of the kidney are composed of a variety of different tissues; that all the tissues develop from a cell tissue that does not show any of the known differentiating marks. Glandular elements are always present, and smooth and striated muscle, cartilage, fat and elastic, fibrous and myxomatous tissue are usually present.

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6. Kretschmer, H. L., and Hibbs, W. G.: Mixed Tumors of the Kidney in Infancy and Childhood: A Study of Seventeen Cases, Surg. Gynec. Obst. **52**:1 (Jan.) 1931.

Embryonal tumors of the kidney are the most common primary neoplasms that occur in children. The largest tumor in Kretschmer's series weighed 1,530 Gm. and the smallest, 235 Gm.; the average weight of all of the tumors was 762 Gm. The tumors are predominately unilateral; only 2 of the 17 reported were bilateral. They are encapsulated and retroperitoneal, and arise within the renal capsule. They are globular to oval in shape, solid, opaque and variously subdivided into lobules. Somewhere on the surface a nodule of renal tissue usually remains. The most distinguishing feature of these tumors is their embryonal structure, with a variety of tissue of abortive renal elements. The types of cells and the amount vary in the different tumors. They are usually myxomatous tissue composed of masses of polymorphous, nucleated cells in which are embedded glandlike or ductlike figures resembling uriniferous tubules, which may be sparse or abundant. There are both epithelial and connective tissue elements. The epithelial elements consist of small and large undifferentiated cells which are often spoken of as epithelial cell nests and embryonal tubules. The connective tissue elements consist of loose stroma, undifferentiated round cells and striated and nonstriated muscle fibers.

Extensions and metastases of such tumors are exceptional unless the original tumor is large. Regional involvement by extension is the usual method of growth. Extension and metastasis may occur throughout the entire abdomen. The time that elapsed between the first noticeable symptoms and the physician's examination was usually short; this varied from six days in one case to twelve months in another. Gross blood in the urine was not found in any of these cases. An increase of temperature is often found with malignant tumors in the adult; fever was present in 9 of the 17 cases, and in all a palpable tumor was present. In all but 1 case, the presence of the tumor was directly responsible for the patient's seeking medical attention. Albumin was present in 7 cases; microscopic blood was found in only 1 case. In every case there was definite evidence of secondary anemia. Of the 17 patients, 16 died.

Bowen and Bennett [7] stated that squamous cell carcinoma of the renal pelvis is not common; among the malignant tumors arising from the epithelium in this region, it is much less common than the papillary types. In 1927, 35 cases of renal tumor were reported from Peter Bent Brigham Hospital; 5 of the tumors originated in the pelvic epithelium; 2 of these were associated with other types of growth, a third was of the papillary type, but none was associated with stone.

7. Bowen, J. A., and Bennett, G. A.: Squamous Cell Carcinoma of the Kidney Pelvis, J. Urol. **24**:495 (Nov.) 1930.

At the time of the report, 9 of the 35 patients were alive, and only 1 of these, with the papillary type of tumor, had suffered from a growth in the renal pelvis.

Bowen and Bennett reported the case of a man, aged 57, with squamous cell carcinoma of the renal pelvis. For many years urinary infection, and for at least a year a renal stone, appeared to be present. Operation revealed moderate pyonephrosis, a branching stone and tumor of the renal pelvis. A recurrence was noted several months later. This case emphasizes the danger of neglecting urinary infections.

[COMPILERS' NOTE.—Squamous cell tumors of the renal pelvis probably result, in most cases, from chronic irritation; they are highly malignant, rapidly involve the renal parenchyma and neighboring tissues and metastasize readily. This type of growth is sometimes, as in Bowen and Bennett's case, associated with renal calculi, which may be rough, irregular and very large. Owing to the absence of symptoms suggestive of a malignant condition, these tumors are rarely seen when the growth is small or localized to the renal pelvis. The operative mortality is high, and most patients who survive die shortly after the operation from local recurrences, or metastatic growths.

Four of 5 cases of squamous cell tumors of the renal pelvis observed at the Mayo Clinic between 1907 and 1922 were associated with renal stone; the calculi in 3 kidneys were extremely large and of the staghorn type. One patient died eight days after operation, and 3 died during the first four months. The fifth patient was alive without symptoms of recurrence six months after operation.]

Graham [8] stated that renal neoplasms occur at all ages, more than 50 per cent occurring in the fourth and fifth decades. The type of tumor of the kidney described by Grawitz is the most common and the most significant. Hypernephroma rarely occurs in children, but is the prevailing type of renal neoplasm in adult life. It is observed more frequently in men than in women. It may be situated in any part of the kidney, but is most often in the upper pole. It is rarely bilateral. Many of the smaller lesions are partially or completely encapsulated. In such cases the tumor increases by local growth without invasion of the surrounding renal tissue. The renal parenchyma may become atrophic as the result of compression. On gross examination, hypernephromas may appear as circumscribed, encapsulated, or diffusely infiltrating masses. They are usually soft and light yellow, and are frequently complicated by varying degrees of diffuse hemorrhage and necrosis.

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8. Graham, Allen: Pathology of Renal Tumors, Radiology **15**:531 (Nov.) 1930.

Second in order of frequency and significance among renal neoplasms are carcinomas, which may be considered in two groups: those arising from tubular or glandular epithelium and those arising from the pelvic mucosa. Adenomas are not infrequently encountered at necropsy as single or multiple lesions in one or in both kidneys. They are generally small, white, circumscribed, nonencapsulated nodules not exceeding 1 cm. in diameter. When the adenoma becomes malignant, fairly well circumscribed or diffusely infiltrating, neoplasms of considerable size may result. Carcinoma of the kidney in childhood is usually a different type and apparently has a different origin from carcinoma in adults. It is generally more undifferentiated or embryonal, and in many cases it seems to be teratomatous, with one type of tissue predominant. The growth may be rapid and large tumors may form, but with little tendency to distant metastasis. Carcinomas arising in the renal pelvis are of two types, papillomatous and epidermoid. A true epidermoid carcinoma with keratohyaline material and pearl formation may arise in the pelvis of the kidney, the seat of leukoplakia. The kidney is infiltrated, and the usual mode of metastasis is through the lymphatics. These tumors are relatively infrequent; they are usually found in chronically infected kidneys or in association with calculus.

True sarcoma in the sense of a malignant tumor arising from the supporting tissue is rarely observed in the kidney as a primary tumor. A search of the records of the Cleveland Clinic for the last eight years failed to disclose a case.

Mixed tumors, the third type of renal neoplasms in order of frequency and significance, are not homogeneous and do not conform to type. Usually they grow rapidly, form large, clinically detectable masses, are difficult to distinguish from pararenal, retroperitoneal and intraperitoneal tumors, and show little tendency to disseminate distant metastasis. On microscopic examination, their structure is found to be extremely variable. The tissues are rarely of a single uniform type. Many of the tumors are radiosensitive and may be kept under control for a considerable period by the application of roentgen rays. The response to irradiation depends, as in the case of tumors generally, on the degree of undifferentiation. Metastatic and recurrent tumors also are radiosensitive in some instances.

Roentgenograms of the kidney indicate the relative size, position and contour of the organ, and show relative variations in the density of the shadow of one portion of the kidney as contrasted with that of another, or of the kidney as contrasted with its surroundings. The cooperation that has been established between urologist and roentgenologist accounts in great measure for the high degree of accuracy

achieved in the interpretation of variations from the roentgenogram and pyelogram of the normal kidney.

Patch and Rhea [9] studied the pathogenesis of bleeding of renal tumors. In the examination of serial sections they were unable to demonstrate destruction of the lining of the pelvis by a tumor, and felt justified in concluding that the hematuria resulted from widely dilated, thin-walled blood vessels in the subepithelial connective tissue of the small protrusion into the superior calix.

*Tuberculosis.*—Spitzer [10] stated that the absence of the bacillus of tuberculosis in the secretion from a kidney does not mean that tuberculosis of the kidney does not exist. The presence of the bacillus in the urine indicates that a focus of tuberculosis is present in either the genital or the urinary tract, as these bacilli do not pass through normal renal epithelium. The experience of careful observers has demonstrated that there is a better chance that patients with tuberculosis of the kidney will recover from other conditions, if the diseased kidney is removed. Tuberculous lesions elsewhere in the body are not a contraindication to nephrectomy; in the majority of cases these are improved after nephrectomy. Regional and spinal anesthesia should be used when possible.

Progressive illness and eventually death are the rule in cases in which nephrectomy cannot be performed for tuberculosis of the kidney. The excellent results obtained following nephrectomy in well selected cases of renal tuberculosis warrant and make imperative its practice whenever possible. If nephrectomy is performed the remainder of the genital and urinary tracts rarely become infected, whereas when nephrectomy is contraindicated, the other parts of such tracts frequently become tuberculous. Other treatment than nephrectomy for tuberculosis of the kidney is not known.

[COMPILERS' NOTE.—That tuberculous bacilluria may exist without renal tuberculosis finds fewer and fewer advocates in the literature. The question of whether nephrectomy is always the procedure of choice in unilateral renal tuberculosis, which was formerly almost universally accepted, is not so easily answered. Thomas has provided much to think about on this subject during the last few years. Perhaps in a few early cases that can be carefully controlled under hospital conditions from month to month, medical treatment may be advisable. However, Spitzer undoubtedly voiced the general opinion in advocating early

9. Patch, F. S., and Rhea, L. J.: On the Pathogenesis of Bleeding in Tumours of the Kidney, Brit. J. Urol. **2**:248 (Sept.) 1930.

10. Spitzer, W. M.: Indications and Contra-Indications for Nephrectomy in Renal Tuberculosis, J. Urol. **24**:469 (Nov.) 1930.

nephrectomy in these cases. When performed early, nephrectomy obviates spread of the infection to other parts of the urinary tract, and in the majority of cases definite cure can be established. In the presence of genital tuberculosis, and especially of bilateral renal tuberculosis, surgical procedures are not nearly so definitely indicated.]

*Actinomycosis.*—Recht [11] stated that there are only 8 reported cases of actinomycosis of the kidney. Israel reported 2 cases. Stanton, Kunith and Kleinschmidt each reported a case in which actinomycotic processes were not present elsewhere. In 2 cases reported by Earl and Abbott there were processes in the brain, lungs and spinal column in addition to those in the kidney. Stanton's and Earl and Abbott's cases were proved at necropsy; the remainder were identified at operation. In Cohn's case actinomycotic spores were found in the urine associated with pyelonephritis and prostatitis. It was thought that infection took place as a result of trauma.

Recht cited the case of a man, aged 65, with arteriosclerosis, chronic nephritis and cystopyelitis. The patient died, and at necropsy actinomycotic nephritis with abscess was found. Search for a primary focus revealed an abscess in the cuneiform bone. The infection of the urinary tract was thought to have been carried to the kidney by the blood stream.

In primary renal actinomycosis Recht noted certain characteristics which later seemed to disappear. The actinomycotic process localized first in the medullary portion of the kidney. General actinomycosis followed, and later the kidney became infected. Cortical abscesses were noted before involvement of the medullary portion.

[COMPILERS' NOTE.—The rarity of renal actinomycosis as a primary or a secondary disease is emphasized. The diagnosis will rest on finding the ray fungus in the urine, or in the tissues at operation. Eisendrath expressed the opinion that operation is contraindicated unless the lesion is well encapsulated; he recommended Bevan's treatment with copper sulphate, potassium iodide and roentgen rays. Three primary cases are on record in which the cure is of long standing (Eisendrath). A single case of primary actinomycosis of the ureter has been noted in the literature (Eisendrath).]

*Movable Kidney.*—Lewis and Carroll [12] stated that every kidney is normally movable, making its excursions up and down with respiration or with movements of the body. The kidney becomes diseased when

11. Recht, Hans: Zur Kenntnisnahme der "isolierten" Nierenaktinomykose, Deutsche Ztschr. f. Chir. **224**:414 (June) 1930.

12. Lewis, B., and Carroll, G.: Clinical Evidence on the Question of Movable Kidney, J. Urol. **24**:479 (Nov.) 1930.

mobility is extreme, or when it becomes displaced and remains in its abnormal position.

Movable kidney demands prompt recognition and appropriate surgical relief. Diagnosis requires proof particularly as to whether the symptoms are from displacement or mobility. Methods of relief are palliative and surgical. Nephropexy affords permanent results when properly carried out. Binders do not cure or afford permanent relief. Fattening methods of treatment are not successful.

Deming [13] stated that nephroptosis is a common condition, but is not always accompanied by symptoms. The coexistence of visceroptosis with nephroptosis is rare; disease of the gallbladder is sometimes associated with movable kidney. Kinks of the ureter are secondary to ptosis, and renal infection occurs in 33.33 per cent of the cases. Conservative treatment is effective in some instances. Deming has devised a new and successful extraperitoneal operation for nephroptosis which does not injure the kidney or its capsule and which utilizes all the natural supporting structures and places the kidney in an anatomically correct position.

*Hydronephrosis.*—Scholl [14] stated that the present tendency of urologic surgeons is to employ the most conservative methods in the treatment for lesions of the kidney whenever such measures are compatible with satisfactory results. It is now possible to utilize the less radical procedures, with the consequent saving of functioning tissue. These procedures are especially applicable in lesions such as bilateral hydronephrosis.

A case is reported in which operation was performed for bilateral hydronephrosis. Nephropexy and decapsulation, with stripping of the renal vessels and freeing of the ureteropelvic angle, were performed on both kidneys. Immediately after operation the pelvic capacity and retention were within normal limits. The patient was active physically, doing a full day's work and living a normal life free from pain or discomfort more than a year after operation. The urine from the bladder contained only a few pus cells and no albumin. The patient had gained more than 50 pounds (22 Kg.) in weight.

*Surgical Technic.*—Holland [15] presented a method of nephrostomy which Cabot has found useful and which has the following advantages:

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13. Deming, C. L.: Nephroptosis, Causes, Relation to Other Viscera, and Correction by a New Operation, J. A. M. A. **95**:251 (July 26) 1930.

14. Scholl, A. J.: Conservative Surgery of Bilateral Hydronephrosis, J. Urol. **24**:251 (Sept.) 1930.

15. Holland, W. W.: A New Method of Performing Nephrostomy: Preliminary Report, Proc. Staff Meet., Mayo Clin. **5**:325 (Nov. 12) 1930.

The nephrostomy tube can be introduced without mobilization of the kidney; it can be quickly and accurately placed in the pelvis with the minimal amount of trauma, and intrarenal hemorrhage can be controlled through pressure of the tube. A uterine probe is bent into a V shape, introduced into the incision in the pelvis, and brought out at the point of election on the convex border of the renal cortex. The uterine probe is used because of its bulbous end and its malleability. A piece of stout thread is attached to the end of the probe which is drawn down and out through the incision in the pelvis and attached to a winged catheter.

Cabot stated that the central requirement of this method is that the tube shall be accurately placed in the renal pelvis without undue destruction of the substance of the kidney. The operation is commonly applied to patients for whom the element of time is important. The common method has been to insert an instrument through the kidney until it is thought to lie in the pelvis of the kidney. By the procedure described, no difficulty is experienced in introducing the tube into the pelvis. It is not necessary to deliver the kidney to perform the operation. A small opening is made in the pelvis, and the probe is introduced and pushed out through the cortex at the point of election. There is no certain point of election to be used as a standard. The tube should come out at the point where it will best drain the kidney. The common complication of nephrostomy is bleeding from the wound. Bleeding may be stopped by pressure. If the hole is larger than the tube, clots may form in the pelvis and thus the whole operation is a failure. By this method the V-shaped end of the catheter slips easily into the hole and the tube fits so snugly that bleeding is entirely controlled. The tube will stay in position as long as necessary. The second great difficulty in the old method comes at the time of insertion of another tube. A tube may be required for months or even permanently. This type of catheter will remain anchored and when a fresh tube is put in it returns with certainty to the original position.

[COMPILERS' NOTE.—Nephrostomy by incision through the renal cortex into the pelvis and subsequent drainage by catheter has too often been marred by hemorrhage into the pelvis. As this procedure interferes with renal function, its purpose may be defeated. Cabot's operation, as described by Holland, seems to offer several advantages in that the kidney need not be disturbed from its bed, a small exposure of the pelvis is necessary, the opening in the parenchyma is made just large enough to admit the catheter, which fits snugly, and the catheter can be accurately guided into the proper position for drainage.]

*Solitary Kidneys.*—Walters and Wright [16] reviewed 52 operations on solitary kidneys and ureters performed at the Mayo Clinic over a period of nineteen years. Solitary kidney occurred twice as often in men as in women; in 75 per cent of the cases patients were in the third or fourth decade. In 45 of the 52 cases, operations were performed for the removal of urinary calculi; in the 7 remaining cases, for conditions other than stone. Of the 45 cases of lithiasis, the stone was removed from the kidney in 34 and from the ureter in 11. There were 6 deaths following removal of stones from the kidney, a mortality of 13.3 per cent. All of the 11 patients from whom stones were removed from the ureter of a solitary kidney recovered. Of these patients, 4 had complete urinary obstruction, and 2 had had anuria, lasting for twenty-four hours after admission. In cases in which operation was performed for stone, pelviolithotomy was done in 24 instances, ureterolithotomy in 10, nephrolithotomy in 7, nephropelviolithotomy in 2, pelvio-ureterolithotomy in 1 case, ureteral meatotomy in 1, and resection of the upper pole of the kidney with removal of stones in 1.

The risk of operation on the solitary kidney is dependent on its function and the degree of infection. Renal function was abnormally low in all of the cases. Delay in operating on a solitary kidney until urinary obstruction with anuria had occurred definitely increased the mortality rate of operations in such cases. Results are somewhat dependent on the size and number of stones present. Reports in the literature and a study of cases seen at the clinic would indicate that in the presence of satisfactory function of the remaining kidney, without abnormal infection, multiple operations can be safely undertaken on the solitary remaining kidney, with the expectation of satisfactory results.

[COMPILERS' NOTE.—The conclusions in a recent paper by Keyes and Mathé on solitary kidneys and ureters are, in general, in agreement with those of Walters and Wright, who have emphasized that the expectancy of good results in operative procedures is dependent on renal function and the degree of infection. It has been shown experimentally that a fourth of the renal parenchyma may adequately take care of renal function, if the remaining tissue is healthy and in condition to function so far as its vascular supply and physiologic drainage are concerned. The urgency for early operation is easily understood in the light of this experimental evidence.]

16. Walters, Waltman; and Wright, William: Operations on Solitary Kidneys and Ureters: Report of Fifty-Two Cases, Surg. Gynec. Obst. **51**:836 (Dec.) 1930.

Mathé [17] stated that the treatment for stone in the solitary kidney and ureter includes such prophylactic measures as the early removal of unilateral calculi and nephrectomy for pyonephrosis due to calculus which might act as a focus for the formation of stone in the healthy kidney, the clearing up of all foci of infection in other portions of the body, the elimination of stasis in the upper and lower parts of the urinary tract, the eradication of infection in the remaining kidney, and a careful regimen with regard to abstinence in eating and drinking.

Five cases of stone in a solitary kidney are reported, the clinical cause of which emphasizes early removal of stone from the single kidney before renal insufficiency and advanced infection have set in and increased the surgical risk. Early lithotomy on the solitary kidney and ureter is a benign operation, followed by practically no shock, and is tolerated as well as by patients with two kidneys. Attempts to induce stones to pass from a solitary renal pelvis or ureter by cystoscopic manipulation are dangerous because the stone, in passing, may obstruct the ureter. Surgical removal of stone from a solitary kidney and ureter requires the most exacting operative technic and keen surgical judgment. Preliminary drainage and lavage should be made through the ureteral catheter. A wide incision assures good exposure. Extreme gentleness should be employed in handling the kidney, blood vessels should not be sacrificed, and the incision in the pelvis and ureter should not be sutured, in order to assure drainage. A combination pyelotomy and nephrotomy incision permits entire removal of a stone and is less likely to be followed by recurrence. Decapsulation should be done to avoid postoperative renal congestion.

### URETER

*Tumors.*—Cerati [18] studied 76 cases of primary epithelial tumors of the ureter; 55 were papillary tumors and 17 were nonpapillary; the nature of the neoplasm could not be determined in 5 cases. From a clinical point of view these tumors are divided into three groups: those situated low, those in the median and superior portions of the ureter and those in both ureters. The evolution depends almost entirely on the histologic type of the tumor. Even in histologically benign tumors the prognosis is serious on account of the accompanying renal lesions. The diagnosis is difficult. Cystoscopy is important because it permits observation of the tumor (visible in a third of the cases),

17. Mathé, C. P.: The Management of Stone in the Solitary Kidney and Ureter, Surg. Gynec. Obst. **52**:79 (Jan.) 1931.

18. Cerati, P.: Contribution a l'étude des tumeurs épithéliales primitives de l'urétère et de leur traitement, Montpelier méd. **45**:126, 1930.

bilateral ureteral catheterization and biopsy. Ureterograms sometimes give definite evidence of the growth of the tumor. Nephro-ureterectomy is the treatment of choice when the corresponding kidney functions satisfactorily and the general condition of the patient permits. If complete nephro-ureterectomy cannot be performed, one of several other procedures may be indicated, such as low resection of the ureter outside or through the bladder with ureteroneocystostomy, resection with suture end to end, or fixation to the skin, transvesical resection of a pediculated tumor or diathermization by the endovesical route.

Ockerblad and Helwig [19] stated that primary carcinoma of the ureter is rare; Meeker and McCarthy reviewed only 33 cases up to 1923. Kretschmer reported a case in 1922. Ochsner had reviewed 47 cases of primary tumor of the ureter, both benign and malignant. Since 1923, Ockerblad and Helwig have reviewed approximately 18 cases and reported a case of their own. Primary carcinoma of the ureter is still a rare disease, but owing to increasingly careful necropsies and skillful urologic diagnosis, more cases continue to be reported. If the growth in the ureter is discovered in its early stages, successful operation and cure are not impossible. The symptoms are obscure and variable; hematuria is a reliable symptom. The diagnosis can be made by a ureterogram which shows a dilation or filling defect in the ureter.

[COMPILERS' NOTE.—A primary malignant growth in the ureter is rare. The distinction of secondary neoplasms from the renal pelvis and also from inflammatory granulomas, as described by Braasch, may offer difficulties even with cystoscopy and ureterography. Hematuria, a localized filling defect shown in the ureterogram, and ureteral and pelvic dilatation, constitute the three most reliable criteria in diagnosis. As Cerati pointed out, the ureterogram may sometimes appear normal. Complete nephro-ureterectomy, dissecting out the ureter first (Beer), is the ideal treatment. If the tumor has grown into, or has been transplanted into the bladder, one gains additional diagnostic evidence and the surgical attack is directed first on the bladder and the lower part of the ureter. Here ureteroneocystostomy or transplantation of the proximal portion of the ureter into the skin may be necessary at the primary operation.]

Rohrer [20] reported a case of primary papillary epithelioma of the ureter, in which there were typical symptoms. Implants occurred from above downward, in the direction of the urinary stream. When nephrec-

19. Ockerblad, N. F., and Helwig, F. C.: Primary Carcinoma of the Ureter, J. Urol. **24**:451 (Nov.) 1930.

20. Rohrer, P. A.: Papillary Epithelium of the Ureter, J. Urol. **24**:639 (Dec.) 1930.

tomy is contemplated for renal papilloma or tumor in the upper part of the ureter, it is advisable to remove the ureter in toto, either at the time of nephrectomy or as soon after as the patient's condition permits.

*Stone.*—Crane [21] reported a case in a man in whom a large ureteral calculus formed rapidly. The stone was 4.5 cm. long and formed during a period of seven months. This case illustrates the rapidity with which large calculi may recur in the urinary tract and the futility of treatment unless the source of the trouble is found and removed. Correlating the history, operative data and subsequent course of the patient, it may be assumed that a chronic progressive infection in the kidney was the primary source of the stone.

[COMPILERS' NOTE.—A rapidly growing ureteral stone is of unusual interest. Generally ureteral stones enlarge slowly and may remain the same size for years. Stones in the pelvis of the kidney also develop slowly. Two cases observed over a period of years showed an increase in size of about 20 per cent a year. Rapidly growing stones in the bladder are not infrequently seen; usually they are of the soft, phosphatic type. In a case observed, a stone 5 cm. in diameter developed in a period of five weeks between the two stages of a prostatectomy.]

Squires [22] stated that the removal of calculi from the ureter by cystoscopic manipulation or operative cystoscopy has been greatly simplified since this procedure was instituted in 1915. At that time each patient was treated intensively and hospitalized. As a result the reactions and symptoms that occasionally followed cystoscopic manipulation were numerous. The patients are now treated at longer intervals and the catheter is not allowed to remain in the ureter so long; often it is left in place only a few hours, whereas previously it was left in from twenty-four to seventy-two hours. When there is impaction with obstruction and pelvic retention, the catheter is left in place for from twenty-four to seventy-two hours.

The plan of procedure as outlined by Crowell consisted in ureteral dilatation, ureteral anesthesia and lubrication. A 2 per cent solution of procaine hydrochloride is used as an anesthetic; it is allowed to remain in the ureter or renal pelvis for a period of twenty minutes and then is drained; as the ureteral catheter is withdrawn, sterile liquid petrolatum is injected.

In 606 cases of ureteral calculi, 528 calculi were recovered by cystoscopic manipulation and 44 by open operation. In 22 cases the

21. Crane, Whitfield: Rapid Formation of Large Ureteral Calculus with Recurrent Bladder Stone, J. Urol. **24**:463 (Nov.) 1930.

22. Squires, C. B.: Disposition of Ureteral Calculi at the Crowell Clinic from 1915 to March 31, 1930, J. Urol. **24**:461 (Nov.) 1930.

stone was not recovered. In the majority of cases of cystoscopic manipulation the calculi passed following treatment.

*Ureteral Transplantation.*—Sisk, Wear and O'Brien [23] reported on thirty-one operations of transplantation of ureters to the sigmoid in 29 dogs. The transplantation was highly unsatisfactory by the Mayo technic. In every case the kidney became infected and closure of the ureterosigmoidal opening by the mucosa of the bowel occurred in five of the seven unilateral transplants. In the 2 cases of bilateral transplants the ureteral openings were markedly stenosed. The Coffey technic gave slightly better results. Complete closure of the ureteral opening occurred in only one ureter. With the unilateral Coffey operation there was no microscopic evidence of pyogenic infection, yet the dogs did not appear to be well after the operation.

Solution of the problem of preventing ascending renal infection probably depends on the discovery of means to prevent infection through the lymphatics. They obtained partial success in this regard in cases in which the exposed end of the ureter was protected for a time from infected material. Until a uniformly successful procedure is evolved, it would seem better to transplant the ureter only in those cases in which older and better understood methods cannot be employed.

*Kinks.*—Thompson and Bumpus [24] called attention to the possibility of producing a kink in the ureter during pyelography when the roentgenogram is made during deep inspiration. They stated the belief that this is the possible explanation of why they were unable to demonstrate such kinks in many cases in which a diagnosis of ureteral kink had been given elsewhere. Three of the cases presented by these authors showed a ureteral kink when the exposure was made during full inspiration and absence of the kink during full expiration.

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23. Sisk, I. R.; Wear, J. B., and O'Brien, H. A.: Transplantation of the Ureters to the Sigmoid: An Experimental Study in Dogs, Surg. Gynec. Obst. **52**: 212 (Feb.) 1931.

24. Thompson, G. J., and Bumpus, H. C., Jr.: Ureteral Kinks: How They Occur at the Order "Take a Deep Breath and Hold It," J. A. M. A. **94**:771 (March 15) 1930.

(*To be Continued*)

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